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Contents

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Contents

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World Journal of Gastrointestinal Surgery (*World J Gastrointest Surg*, *WJGS*, online ISSN 1948-9366, DOI: 10.4240) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

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MINIREVIEWS

Sentinel node navigation surgery in gastric cancer: Current status

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Abstract

The theory behind using sentinel node mapping and biopsy in gastric cancer surgery, the so-called sentinel node navigation surgery, is to limit the extent of surgical tissue dissection around the affected organ and subsequently the accompanied morbidity. However, obstacles on the clinical correspondence of sentinel node navigation surgery in everyday practice have occasionally alleviated researchers' interest on the topic. Only recently with the widespread use of minimally invasive surgical techniques, *i.e.*, laparoscopic gastric cancer resections, surgical community's interest on the topic have been unavoidably reflated. Double tracer methods appear superior compared to single tracer techniques. Ongoing research is now focused on the invention of new lymph node detection methods utilizing sophisticated technology such as infrared ray endoscopy, florescence imaging and near-infrared technology. Despite its notable limitations, hematoxylin/eosin is still the mainstay staining for assessing the metastatic status of an identified lymph node. An intra-operatively verified metastatic sentinel lymph node will dictate the need for further conventional lymph node dissection. Thus, laparoscopic resection of the gastric primary tumor combined with the appropriate lymph node dissection as determined by the process of sentinel lymph node status characterization represents an option for early gastric cancer. Patients with T3 or more advanced disease should still be managed conventionally with resection plus standard lymph node dissection.

Key words: Sentinel node; Gastric cancer; Minimally invasive surgery

Core tip: Sentinel node navigation surgery can change the current surgical treatment of gastric cancer expanding the indications of minimally invasive surgical options such laparoscopic techniques. However, the complex lymphatic drainage of the stomach and the ubiquitous fear of skip metastasis make the selection of patients extremely important. Currently, laparoscopic resection of the tumor from the stomach with lymph node dissection navigated by sentinel lymph node identification represents an option only for early gastric cancer patients. Unfortunately, patients with T3 or more advanced disease should still be managed conventionally with resection plus lymph node dissection.

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INTRODUCTION

Melanoma was the first malignancy that the concept of sentinel node found application for. However, the indications and uses of this attractive procedure have been

Table 1 Lymph node stations of the stomach

Lymph node stations	Anatomic location	Group	Lymphadenectomy
1	Right cardia	N1	D1
2	Left cardia		
3	Lesser curvature		
4	Greater curvature		
4a	Short gastric vessels		
4b	Left gastroepiploic vessels		
4c	Right gastroepiploic vessels		
5	Suprapyloric		
6	Infrapyloric		
7	Left gastric artery	N2	D2
8	Common hepatic artery		(N1 + N2)
9	Celiac trunk		
10	Splenic hilus		
11	Splenic artery		
12	Hepatoduodenal ligament	N3	D3
13	Posterior surface of the head of the pancreas		(N1 + N2 + N3)
14	Root of the mesentery		
14A	Superior mesenteric artery		
14V	Superior mesenteric vein		
15	Para-aortic	N4	D4
16	Paracolic		(N1 +N2 + N3 +N4)

recently expanded in many fields of surgical oncology such as breast cancer, thyroid cancer, gynecological malignancies, colorectal and, recently, gastric cancer. Sentinel node mapping and biopsy in gastric cancer surgery, the so-called sentinel node navigation surgery, aimed to limit the extent of surgical tissue dissection around the affected organ. By convection, any unnecessary dissection, *i.e.*, dissection of virgin-tumor free areas unrelentingly increase morbidity without always respective survival benefits. Within this context, sentinel lymph node navigation surgery could, at least theoretically, facilitate precise and sufficient resections. However, in some instances, insurmountable obstacles on the clinical correspondence of the sentinel node navigation surgery concept in everyday practice have occasionally alleviated researchers' interest on the topic. Only recently with the widespread use of minimally invasive surgical techniques, *i.e.*, laparoscopic gastric cancer resections, surgical community's interest on the topic have been unavoidably reflated.

Nowadays, the following questions regarding the utility of sentinel lymph node mapping and biopsy in clinical practice need to be precisely answered: (1) which are the available techniques for sentinel lymph node mapping? (2) which is the best way to administer the tracer? (3) which is the optimal method to verify the presence of metastasis in the identified sentinel lymph node? (4) which is the gastric cancer patient subgroup suitable for sentinel node mapping and biopsy? and (5) which are the available options for primary tumor control?

LYMPH NODE STATIONS

In 1973, the Japanese Research Society for the study of gastric cancer published a manual standardizing lymph node dissections in gastric cancer by recognizing 16 distinct anatomic lymph node stations. Further grouping of these lymph node stations took place, *i.e.*, N1, N2, N3 and N4 to achieve correspondence with respective lymph node dissection extents, *i.e.*, D1, D2, D3 and D4[1] (Table 1).

LYMPHATIC STREAM IN GASTRIC CANCER

Trying to decipher the lymph route out of a malignant lesion within the stomach, a few anatomical considerations are of paramount importance. Briefly, from the anatomic viewpoint, lymph from the gastric wall is drained *via* lymphatic vessels which form a complex sub-peritoneal plexus surrounding the stomach both anteriorly and posteriorly. Depending on the location, the lymph of the upper left part of the stomach is routed to the left gastric and pericardial nodes. Lymph originated from the pylorus is filtered through the supra-pyloric and the right supra-pancreatic nodes. The region of the fundus filters lymph along the gastrosplenic ligament and splits with lymph flowing to the left supra-pancreatic nodes and the left gastroepiploic nodes via the splenic nodes. Lymph from the pyloric and the distal portion of the corpus collects in the right gastroepiploic nodes and then flows to the sub-pyloric nodes. From all regions, the lymph stream continues to the celiac nodes[1].

When dealing with malignant lesions, clarifying the lymphatic drainage pattern is crucial for performing proper lymph node dissections especially from sites "susceptible" to metastasis. However, as briefly discussed above, the lymphatic stream of the stomach appears particularly complex and multidirectional and in many occasions ill-investigated. Certainly, having even a rough idea of how lymph drains out of the stomach will render upper gastrointestinal (GI) surgeons capable of performing effective and, up to a point, targeted lymph node dissections[2]. Nevertheless, tumors at any location within the stomach have a non-negligible chance of atypical metastasis. Tumors located longitudinally or circumferentially in the lower part of the lesser curvature appear to be of higher chance for an atypical metastasis compared to other locations[3]. It becomes obvious that the efficiency of the sentinel node concept is compromised when dealing with tumors at these locations as an unacceptable increase of false-negative results should be anticipated. Studies raise the incidence of skip metastasis up to 29%[3]. Apart from the location, the degree of tumor differentiation has been inconsistently implicated as to increase skip metastasis potential[4].

Generally, the severity of gastric malignancy, *i.e.*, tumor size and depth of invasion is positively correlated with the lymph node metastasis rate[5]. In addition, studies using a retrospective methodology and including patients with sole lymph node involvement have shown that the majority of sentinel lymph nodes are located in the regional area at a close proximity to the tumor[6]. It is recommended, that if nodes are not identified in the usual locations, then No. 7, 8 and 9 lymph node stations should

be investigated as well[7].

WHICH ARE THE AVAILABLE TECHNIQUES FOR SENTINEL LYMPH NODE MAPPING?

Numerous methods in order to increase the usefulness and effectiveness of sentinel node mapping have been proposed to date[8-18]. The clinical evaluation and assessment of these modalities within studies have led to a breathtaking progress in the field rendering sentinel lymph node tracking techniques familiar to surgeons. However, the main problem is on the logistics of each technique. Identifying sentinel lymph nodes intraoperatively in a timely and effective pattern is by definition a challenging process. The tracer used should meet the minimum requirements of (1) non-toxicity; (2) easy availability; and (3) cost-effectiveness. Ideally, the tracer should accumulate within the sentinel nodes for a period of time long enough to render detection possible. Furthermore, it should be readily identifiable without the need for using sophisticated and unfamiliar to surgeons equipment. As no single tracer to date incorporates all of the above characteristics, the quest for the optimal compound seems to be ongoing.

Dye-based and radioisotope-based techniques have been the mainstay for lymph node detection so far[8-18]. Dye agents include isosulfan blue, patent blue and indocyanine green (currently, the most commonly used dye). On the other hand, technetium 99 m represents the most commonly used radioisotope. The use of infrared ray beam *via* endoscopy can, at least theoretically, facilitate the visualization of the used tracer increasing the accuracy of the detection[19,20]. Similarly, fluorescence imaging is another available adjunct which is suggested to increase the detection rates of traditional dye agents such as indocyanine green[21,22].

However, sentinel lymph node mapping of the GI tract by using available techniques is often limited by various factors. The multidirectional lymph drainage patterns and, practically, the inability to image surgical anatomy in real time in relation to the used tracer can compromise the whole process. In this direction, the use of invisible near-infrared light might have the answers. In this technique, an intraoperative near-infrared fluorescence imaging system that simultaneously displays surgical anatomy is utilized. Near-infrared fluorescence images of the surgical field are generated to illustrate intra-parenchymally injected near-infrared fluorescent quantum dots. The final result is the visualization of the draining lymphatic tree and of the nodes as well. The technique promises dissection under real time vision[23].

Generally, there is a trend for combining tracers in order to increase the detection accuracy. Double tracer techniques (dye plus isotope), almost consistently, seem to increase the rate of sentinel lymph node identification[24-30], however there are indeed studies which question this finding[31,32]. In addition, pre-clinical research is in progress for inventing the optimal tracer and visualization system. It seems pretty likely at this point that research will overcome the traditional dye-based techniques and it will open new perspectives in sentinel node mapping.

WHICH IS THE BEST WAY TO ADMINISTER THE TRACER?

Traditionally, endoscopy has been used in order to inject the tracer sub-mucosally around the primary tumor. The administration was carried out either preoperatively in case of isotopes and intra-operatively in case where a dye was the used tracer. Sub-serosal injection of dye has been tested, as well, without however notably superior results compared to the standard sub-mucosal injection[33,34].

WHICH IS THE OPTIMAL METHOD TO VERIFY THE PRESENCE OF METASTASIS IN THE IDENTIFIED SENTINEL LYMPH NODE?

The traditional practice of sentinel node biopsy for gastric cancer has been largely based on the use of hematoxylin and eosin (HE) staining for histological examination of frozen section slices. As the accuracy of intraoperative diagnosis of metastasis based on Hematoxylin/Eosin staining ranges significantly in the literature (74%-100%), the issue of whether this certain staining is efficient as a standalone modality remains controversial[35-42]. Because of this controversy, efforts have been directed towards identifying more reliable histopathological methods. Immunohistochemical staining and reverse transcription-polymerase chain reaction have been both tested in this direction yielding a significantly higher metastasis detection rate than the standard staining technique.

Having this comparative principles, Arigami *et al*[43] reported the following metastatic detection rates: 8.2% for hematoxylin/eosin, 13.1% for immunohistological staining and 36.1% for reverse transcriptase polymerase chain reaction. These major differences in the detection rates can be explained by the fact that the more sensitive and sophisticated the technique used is, the more likely the detection of micrometastasis is. As the prognostic significance of micrometastasis in gastric cancer has yet to be confirmed, the aforementioned differences require careful interpretation. However, whatever the natural history of gastric cancer micrometastasis is, the widespread use of these sophisticated techniques is quite problematic. Firstly, the penetrability of these techniques among institutions is still poor because of the unavailability of the technical equipment. Secondly, due to the logistics, obtaining a definite result in a timely manner, *i.e.*, before the end of the procedure is still mainly futile. Thus, despite its limitations hematoxylin/eosin staining remains the standard method for examining the detected sentinel

lymph nodes.

WHICH IS THE GASTRIC CANCER PATIENT SUBGROUP SUITABLE FOR SENTINEL NODE MAPPING AND BIOPSY?

Although attractive as a concept, sentinel node biopsy is indicated only for a strict subgroup of gastric cancer patients. Depending on the geographic distribution of each study's institution, eligibility ranges from 3% to 50% of all gastric cancer patient population[44-47]. Eastern studies have included clinically node-negative T1 and T2 patients[48-51]. On the other hand, studies originating from Western institutions have included T3 tumors as well[52]. The complex lymphatic drainage of the stomach and the ubiquitous fear of skip metastasis make the selection of patients extremely important. Fortunately, skip metastasis is encountered usually within the same group of nodes as the identified sentinel lymph node. An approach of removing the entire group of nodes rather than focusing on the identified represents the safest choice[28,53].

WHICH ARE THE AVAILABLE OPTIONS FOR PRIMARY TUMOR CONTROL?

The "less invasive" theory behind sentinel lymph node biopsy has its benefits based on the limitation of morbidity caused by unnecessary dissection. At least theoretically, combining the method with minimally invasive surgical procedures such as laparoscopic surgery sounds attractive. Studies have already tested the sentinel node concept for both open, laparoscopic gastrectomies and even natural orifice transluminal endoscopic surgery[54-56]. Generally, there is no consensus regarding the optimal primary tumor control during sentinel node navigation surgery[57]. Endoscopic resection may be safely applied to small mucosal cancers, but other surgical options such as minimally invasive function-preserving resection of the stomach should be employed for larger lesions, given their tendency for diffuse invasion[57].

CONCLUSION

In conclusion, sentinel node navigation surgery can change the current surgical treatment of gastric cancer. The applications and ultimately the indications of minimally invasive surgical options such as laparoscopic techniques can be significantly expanded and boosted with the generalized use of sentinel node navigation surgery. Currently, the double tracer method (indocyanine green and radio-isotope tracers) appears to be the method of choice due to its increased efficacy in detecting nodes compared with single tracer techniques. Research is focused on the invention of new lymph node detecting methods utilizing infrared ray endoscopy, florescence imaging and near-infrared technology. Despite its limitations and given that the use of more sophisticated techniques is still in a developing stage, hematoxylin/eosin remains the standard staining for assessing the metastatic status of a detected lymph node.

An intraoperatively detected metastasis of a sentinel lymph node is the factor that will determine whether a patient will proceed with conventional lymph node dissection or not. Laparoscopic resection of the tumor from the stomach with lymph node dissection navigated by sentinel lymph node identification represents an option only for early gastric cancer patients. Unfortunately, patients with T3 or more advanced disease should still be managed conventionally with resection plus lymph node dissection.

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RETROSPECTIVE STUDY

Pathological factors affecting gastric adenocarcinoma survival in a Caribbean population from 2000-2010

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Abstract

AIM: To investigate pathological factors related to long term patient survival post surgical management of gastric adenocarcinoma in a Caribbean population.

METHODS: This is a retrospective, observational study of all patients treated surgically for gastric adenocarcinoma from January 1st 2000 to December 31st 2010 at The University Hospital of the West Indies, an urban Jamaican hospital. Pathological reports of all gastrectomy specimens post gastric cancer resection during the specified interval were accessed. Patients with a final diagnosis other than adenocarcinoma, as well as patients having undergone surgery at an external institution were excluded. The clinical records of the selected cohort were reviewed. The following variables were analysed; patient gender, patient age, the number of gastrectomies previous performed by the lead surgeon, the gross anatomical location and appearance of the tumour, the histological appearance of the tumour, infiltration of the tumour into stomach wall and surrounding structures, presence of *Helicobacter pylori* and the presence of gastritis. Patient status as dead *vs* alive was documented for the end of the interval. The effect of the aforementioned factors on patient survival were analysed using Logrank tests, Cox regression models, Ranksum tests, Kruskal-Wallis tests and Kaplan-Meier curves.

RESULTS: A total of 79 patients, 36 males and 43 females, were included. Their median age was 67 years (range 36-86 years). Median survival time from surgery was 70 mo with 40.5% of patients dying before the termination date of the study. Tumours ranged from 0.8 cm in size to encompassing the entire stomach specimen, with a median tumour size of 6 cm. The median number of nodes removed at surgery was 8 with a maximum of 28. The median number of positive lymph nodes found was 2, with a range of 0 to 22. Patients' median survival time was approximately 70 mo, with 40.5% of the patients in this cohort dying before the terminal date. An increase in the incidence of cardiac tumours was noted compared to the previous 10 year interval (7.9% to 9.1%). Patients who had serosal involvement of the tumour did have a significantly shorter survival than those who did not (P = 0.017). A significant increase in the hazard ratio (HR), 2.424, for patients with circumferential tumours was found (P = 0.044). *Via* Kaplan-Meier estimates, the presence of venous infiltration as well as involvement of the circumferential resection margin were found to be poor prog-

nostic markers, decreasing survival at 50 mo by 46.2% and 36.3% respectively. The increased HR for venous infiltration, 2.424, trended toward significant (P = 0.055) Age, size of tumour, number of positive nodes found and total number of lymph nodes removed were not useful predictors of survival. It is noted that the results were mostly negative, that is many tumour characteristics did not indicate any evidence of affecting patient survival. The current sample, with 30 observed events (deaths), would have about 30% power to detect a HR of 2.5.

CONCLUSION: This study mirrors pathological factors used for gastric cancer prognostication in other populations. As evaluation continues, a larger cohort will strengthen the significance of observed trends.

Key words: Gastric adenocarcinoma; Caribbean; Jamaica; Pathologic; Survival; Gastrectomy; Gastritis; *Helicobacter pylori*; Cardia; Circumferential resection margin

Core tip: This ten year retrospective analysis of pathologic factors affecting the survival of gastric cancer patients is the first ever to be done in a Caribbean population. Significant findings meriting publication include increasing incidence of proximal tumours and decreased survival with involvement of the circumferential resection margin. Among other factors also examined, are the impact of surgeon and pathologist training on patient survival. By describing the current state of gastric cancer management in this population, this study aspires to lay the foundation for further work enhancing gastric cancer care in this region.

Roberts PO, Plummer J, Leake PA, Scott S, de Souza TG, Johnson A, Gibson TN, Hanchard B, Reid M. Pathological factors affecting gastric adenocarcinoma survival in a Caribbean population from 2000-2010. *World J Gastrointest Surg* 2014; 6(6): 94-100 Available from: URL: http://www.wjgnet.com/1948-9366/full/v6/i6/94.htm DOI: http://dx.doi.org/10.4240/wjgs.v6.i6.94

INTRODUCTION

Gastric cancer is the fourth most common malignancy in men, and the fifth commonest in women diagnosed worldwide[1]. In Jamaica it is the seventh commonest cancer in men and the ninth most common in women[2]. Worldwide, gastric cancer is the third most frequent cause of cancer death in men and the fifth most common in women[1]. In Jamaica it is the fourth leading cause of cancer related death[3].

These figures prompt scrutiny and characterization of the Jamaican gastric cancer patient population. Accordingly, Plummer *et al*[4] had previously outlined age and sex related incidence, histological appearance, as well as tumour location in a surgically treated cohort of gastric adenocarcinoma patients in Jamaica from 1993-2002, and found that the antrum of the stomach was most often involved, with a trend toward increased incidence of more proximal tumours in the latter 5 years studied, and that lymph node metastases were common[4].

It was our aim to build on this base of information and to explore prognostication in this patient demographic. Our study seeks, for the first time in the Jamaican population, to describe the post-surgical survival rate of gastric adenocarcinoma patients and to elucidate related pathological factors.

MATERIALS AND METHODS

This retrospective, observational study summarizes the analyses conducted on patients diagnosed with gastric adenocarcinoma at the University Hospital of the West Indies (UHWI) from 2000 to 2010. Analysis was conducted using STATA 9. Approval was granted from the Ethics Committee of the hospital (file number ECP334, 12/13). This study was carried out in accordance with the Second International Helsinki Declaration[5].

All patients who were diagnosed with gastric cancer at UHWI during the period January 1st 2000 to December 31st 2010 were enrolled *via* review of pathology reports. UHWI is a type A teaching hospital and a referral centre, accepting the management of patients exceeding the resource capability of several smaller hospitals throughout Jamaica. These patients had all been seen at the General Surgery outpatient clinic, and subsequently undergone upper gastrointestinal endoscopy with biopsy proving gastric cancer. Other forms of gastric cancer besides adenocarcinoma were excluded. Patients with a final diagnosis of gastric adenocarcinoma, but who had undergone surgery at other institutions were excluded. This exclusion came as a matter of access to the clinical records of those patients. Demographically, the patients receiving definitive management at external institutions are not anticipated to greatly differ from the patient population investigated in this study. Of note, the population of Jamaica is predominantly Afro-Caribbean.

Survival data was analysed with the event being death and the time to death being defined as the time in months from surgery until the patient's death. Persons who did not die were censored at the date of their last visit or if confirmed to be alive, they were censored at December 31, 2011.

Logrank tests were conducted to determine whether the survival rate was different across various groupings within variables. Cox regression models were built to determine whether various pathological characteristics would be able to predict a person's risk of death. Rank-sum tests as well as Kruskal-Wallis tests of association were done to determine whether the relationships between clinicopathological factors and survival were different for persons who were dead as opposed to confirmed alive or censored prior to the end of the studied interval[6,7].

Table 1 Clinical characteristics

Characteristic		*n* (%)
Gender	Male	36 (45.6)
	Female	43 (54.4)
Number of previous gastrectomies	< 10	30 (38.0)
by surgeon	> 10	49 (62.0)
Patient status	Alive	7 (8.9)
	Censored	40 (50.6)
	Dead	32 (40.5)

RESULTS

The surgical notes and pathological reports of the 79 patients meeting the criteria of histologically identified gastric adenocarcinoma, and having had D1 gastrectomy at UHWI were reviewed. There were more females (54.4%) than males (Table 1). The median age of the patients was 67 years with a range of 36 to 86 years. Tumours ranged from 0.8 cm in size to encompassing the entire stomach specimen, with a median tumour size of 6 cm. The median number of nodes removed at surgery was 8 with a maximum of 28. Four specimens included 15 or more lymph nodes. Seventy-seven specimens were found to have nodal metastasis. The median number of positive lymph nodes found was 2, with a range of 0 to 22. Patients' median survival time was approximately 70 mo, with 40.5% of the patients in this cohort dying before the terminal date (Table 1). A total of 47 patients were censored, with 7 of those being censored at the end of the study, *i.e.*, confirmed to be still living as at December 31, 2011.

In this series, thirty-eight percent of the surgeries were performed by doctors who had performed less than 10 gastrectomies, while the other 62% were performed by surgeons who had performed 10 or more (Table 1) . Approximately a quarter (24.7%) of patients had tumours situated on the lesser curvature of the stomach while about half that number (11.7%) had tumours involving the greater curvature. The most common anatomical location was the antrum (54%), followed by the pylorus (37.7%). Fifteen point six percent of patients had tumours located on the anterior wall of the stomach, 24.7% on the posterior wall, and 16.9% were circumferential (Table 2).

Histologically, less than half of the patients had tumours that were diffuse, while a little more than half (57.4%) were intestinal. Most (43.2%) patients had low grade tumours compared to 32.4% having tumours of moderate grade and the remainder of high grade. More than half of the patients had ulcerative lesions. Few (5.7%) had tumours that were well differentiated, while the majority (50.9%) of patients had tumours that were moderately differentiated. Ninety-six percent of tumours were advanced with involvement of muscularis propria, subserosa and serosa. Forty-eight percent of the patients had venous infiltration by the adenocarcinoma, while 60% had tumours that exhibited perineural invasion. Approximately 20% of patient specimens had *Helicobacter pylori*. While few (3.8%) patients were found to have chronic active gastritis, about 40% of them had chronic gastritis and about 30% had chronic multifocal atrophic gastritis (Table 3).

Table 2 Tumour location *n* (%)

Location of tumour		*n* = 79
Lesser curvature	Uninvolved	60 (75.3)
	Involved	19 (24.7)
Greater curvature	Uninvolved	70 (88.3)
	Involved	9 (11.7)
Antrum	Uninvolved	35 (45.5)
	Involved	34 (54.5)
Pylorus	Uninvolved	49 (62.3)
	Involved	50 (37.7)
Body	Uninvolved	62 (79.2)
	Involved	17 (20.8)
Cardia	Uninvolved	71 (90.9)
	Involved	8 (9.1)
Fundus	Uninvolved	73 (92.2)
	Involved	6 (7.8)
Anterior wall	Uninvolved	66 (84.4)
	Involved	13 (15.6)
Posterior wall	Uninvolved	59 (75.3)
	Involved	20 (24.7)
Circumferential	Uninvolved	66 (83.1)
	Involved	13 (16.9)

There was a trend toward significance ($P = 0.0577$) in the lower survivorship of patients who had tumours of the gastric cardia *vs* those who did not. Patients who had a circumferential tumour had significantly worse survival times from those who did not have a circumferential tumour ($P = 0.0370$). There was also a near significant difference between patients with subserosal involvement *vs* those without ($P = 0.0731$). Patients who had serosal involvement of tumour did have a shorter survival than those who did not ($P = 0.017$) (Table 4). Patients who had venous infiltration also had shorter survival ($P = 0.055$) (Table 5). Differences for subserosal and serosal involvement could not be quantified as there were no deaths among patients who were negative. Differences in HRs were estimated for tumours of the gastric cardia, circumferential lesions and those with venous infiltration. Figure 1 show the survival curves for the aforementioned variables.

DISCUSSION

The Kaplan-Meier estimated 10-year survival rate of this cohort is 42.1%, with a 95% confidence interval of 24.4%-58.7%. This Kaplan-Meier estimate accounts for the varying risks within the population with respect to their clinicopathological factors. This is appropriate as we have noted statistically significant impact of certain parameters on patient survival. If it were assumed that each patient was at an equivalent risk for mortality following surgery the incidental survival rate would be 35%. The median survival time was about 70 mo. These statistics reflect patients' median follow up time and not a true median survival. Patients were followed for a total of

Table 3 Pathological characteristics

Gross appearance		Percentage
Configuration	Ulcerative	56.00
	Infiltrative	22.70
	Exophytic	21.30
	n	75
Gross location		
Proximal	Uninvolved	88.20
	Involved	11.80
	n	76
Distal	Uninvolved	84.20
	Involved	15.80
	n	76
Histological appearance		
Intestinal	No	42.60
	Yes	57.40
	n	68
Differentiation	Poor	43.40
	Moderate	50.90
	Well	5.70
	n	53
Grade	Low	43.20
	Moderate	32.40
	High	24.30
Maximum extent of invasion through stomach wall		
Mucosa	Involved	100.00
	n	78
Muscularis propria	Uninvolved	3.80
	Involved	96.20
	n	78
Sub–Serosa	Uninvolved	9.00
	Involved	91.00
	n	78
Serosa	Uninvolved	13.30
	Involved	86.70
Histological appearance		
Venous infiltration	Absent	51.90
	Present	48.10
	n	52
Perineural infiltration	Absent	40.00
	Present	60.00
	n	35
H. Pylori	Absent	80.50
	Present	19.50
	n	77
Chronic active gastritis	Absent	96.20
	Present	3.80
	n	78
Chronic gastritis	Absent	59.00
	Present	41.00
	n	78
Chronic multifocal Atrophic gastritis	Absent	70.50
	Present	29.50
	n	78

Table 4 Logrank test of survival functions

Variable	*P* value
Gender	0.9688
Number of gastrectomies previously performed	0.6725
Lesser curvature	0.9716
Greater curvature	0.7928
Antrum	0.2613
Pylorus	0.2486
Body	0.2581
Cardia	0.0577
Fundus	0.9704
Anterior wall	0.3977
Posterior wall	0.9507
Circumferential	0.0370
Diffuse	0.9389
Intestinal	0.6020
Grade	0.2436
Configuration	0.2598
Differentiation	0.2416

1912.115 person months during which time there were 30 deaths. This yields an estimated death rate of 0.0157 deaths per person-month, or 18.8% per person-year (95%CI: 0.132-0.269). This means that if we observed 100 persons with the disease for 1 year we would expect approximately 19 of them to die.

It is noted that the results were mostly negative, that is many tumour characteristics did not indicate any evidence of affecting patient survival. Table 3 shows the results of a power analysis to determine the power of our study to detect varying hazard rates. We see that, at best, the current sample with 30 observed events (deaths) would have about 30% power to detect a HR of 2.5. It is likely that the ability of this study to demonstrate pathological prognosticators already commonly accepted in the literature was limited by this relatively low power. We see that we could detect a hazard rate of 2 with power 80%, if we observed 202 deaths. As the examined cohort continues to grow yearly we can expect more robust statistics in future analyses. Furthermore, this study included all cause mortality. As the cohort continues to grow, exact causes of death can be better examined and adjusted for according to their likely direct relation to gastric cancer and therapeutic intervention for this disease process.

Age, size of tumour, number of positive nodes found and total number of lymph nodes removed were not useful predictors of survival. However, it was noted that patients who had a circumferential tumour were almost two and a half times more likely to die than those without. There was a similar increase in the likelihood of death for patients with tumours of the cardia, as well as in those with venous infiltration (Table 3).

In a previous clinicopathological audit of gastric carcinomas at this institution between 1993-2002, the majority of tumours (56%) were of the antrum. The cardia was the third most involved site at 7.9%[4]. The current study, 2000-2010, noted 9.1% of cases to involve the gastric cardia and 54.5% involving the antrum. While the majority of gastric cancers in our population continue to be found in the antrum, it is worth noting the increased incidence of cancers of the cardia. This early trend parallels the 29.0% to 52.2% increase in incidence of adenocarcinomas of the gastric cardia noted in the United Kingdom from 1984 to 1993[8]. Similarly the incidence of cardiac lesions increased from 29% to 52%, in the United States of America, between 1984-1993[9]. McLoughlin purports a generally poorer prognosis associated with cancers of the gastric cardia as opposed to other anatomical sites[10].

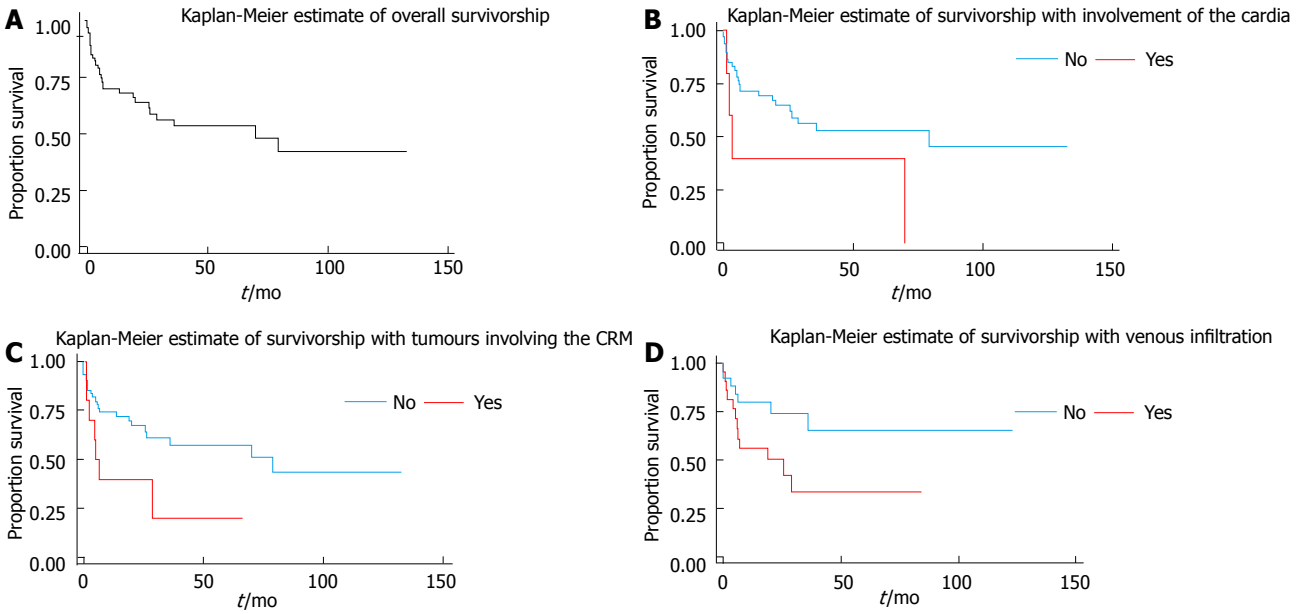

Figure 1 Kaplan-Meier survival. A: Estimate of gastric cancer (2000–2010); B: Estimate of patients with involvement of the Cardia; C: Estimate of patients with tumour involving the circumferential resection margin; D: Estimate of patients with venous infiltration. CRM: Circumferential resection margin.

Table 5 Single predictor cox regression models

Predictor	HR	*P* value	95%CI	
Cardia				
Involved *vs* uninvolved	2.685	0.069	0.927	7.779
Circumferential				
Involved *vs* uninvolved	2.424	0.044	1.025	5.732
Venous infiltration				
Present *vs* absent	2.502	0.055	0.98	6.384
Age	1.007	0.643	0.978	1.037
Size	0.992	0.897	0.877	1.122
Positive lymph nodes	1.059	0.118	0.986	1.137
Total lymph nodes removed	0.981	0.603	0.911	1.055
Type of surgery				
Total gastrectomy *vs* subtotal gastrectomy	1.45	0.417	0.591	3.553
Presence of *Helicobacter pylori*	0.456	0.198	0.138	1.508

This prognosis is likely a consequence of more extensive lymphatic drainage of the region, and later diagnosis[10,11]. In this study a HR of 2.685 (P = 0.069) reflected, although not significantly, this increased risk of mortality. Kaplan-Meier curves demonstrate the decreased survivorship of cardiac gastric cancers in this Jamaican cohort. Finally, the Logrank test trended toward significance with a P value of 0.0577.

This study made evident a significant HR of 2.424 (P = 0.044) for patients with circumferential resection margin (CRM) involvement post-gastrectomy. Logrank survival tests reflect this decreased survivorship with a P value of 0.0370. This applies to cancers of the cardia with extension into the distal oesophagus. CRM involvement has been shown to be an important prognostication factor for oesophageal cancer. Several studies have shown a poor prognosis in patients with potentially resectable malignancies of the distal 5 cm of the oesophagus and Siewert I adenocarcinomas of the gastro-oesophageal junction[12,13]. It would appear that the findings of our study reflect such trends.

As, both globally and locally, more proximal gastric tumour sites become increasingly prevalent, it is important to note the relatively poor outcomes of such cases post gastrectomy. As alluded to above, lymphatic drainage is thought to be a key contributor to such poor outcomes. Accordingly it is prudent to examine the approach to lymph node dissection and excision employed locally, as well as the correlation between lymph node positivity and survivorship. Our study did not demonstrate any significant influence of either lymph node positivity or total number of nodes resected on survivorship. However, Shimada *et al*[14] (2001) with a much larger cohort (982) concluded that the involvement of three or more metastatic lymph nodes is an independent prognostic factor with a sharp decrease in 5-year survivorship of patients with greater than two nodes. An Italian randomised trial involving 615 gastric cancer patients demonstrated significant decrease in all-cause mortality varying proportionately with number of lymph nodes removed up to 25. The authors suggest a minimum of 25 nodes be removed for better long term survivorship[15]. Our study saw an average of only 8 nodes being removed. During this time at our institution the standard procedure performed was that of D1 gastrectomy. This was due to lack of personnel trained in D2 gastrectomy technique. The American Joint Committee on Cancer recommends a minimum of 15 lymph nodes be examined for accurate staging of gastric cancer as retrieved by D2 lymphadenectomy[16]. Only 4 of the 79 specimens reviewed met this recommendation, as D1 gastrectomies were performed. Interestingly, Schoenleber *et al*[17] suggest that the single most influential factor in optimising the number of lymph nodes retrieved, and consequently the number of positive lymph

nodes identified from a gastric specimen, is the technique of the pathology technician in trimming the gross specimen. Thus, the relatively low yield of lymph nodes from the surgical specimens in this study may be a function of either surgeon skill or the technical ability of the pathologist trimming the specimen.

It is important to note that meta-analyses of D1 *vs* D2 lymphadenectomy for gastric cancer have failed to demonstrate any survival benefit of extended resection[18]. The reason for this may be the increased surgical morbidity and mortality that is expected when less experienced staff perform the more technically complex D2 resection classically inclusive of splenectomy and pancreatectomy. At our institution 38% of the reviewed cases had been done by a surgeon who had previously performed less than 10 gastrectomies. No significant change in survivorship was attributable to surgeon experience. The ideal answer to balancing the risk of increased operative morbidity, against the need for oncological clearance of involved nodes, would be to identify involved nodes preoperatively. Currently, algorithms utilising prognostic factors such as age, sex, Borrmann classification and histology are being developed to do just that. The Maruyama computer program was used retrospectively to predict lymph node involvement by level and the results compared to actual pathological specimen findings. The prediction rate was highly accurate (82%-96%)[19]. This high predictive accuracy has been reproduced[20].

This study has also demonstrated an almost significant HR of 2.5 with regard to the survivorship of patients with tumours featuring venous infiltration (P = 0.055). A retrospective analysis, done in China, of 487 gastric cancer patients showed that lymphatic or blood vessel invasion in the presence of metastatic lymph node disease significantly decreased survivorship post gastrectomy[21]. In our study, all but two of the histological specimens had positive nodes, therefore a similar overall trend was observed. Additionally, a study, done in South Korea, of 280 node negative patients demonstrated significant worsened prognosis for patients with blood vessel invasion[22].

Given that there is sufficient evidence in the literature that some of these characteristics are clear indicators of survival, we could conclude that our study lacked the power to sufficiently detect the results. Specifically, a hazard rate of 2 with power of 80 would require 202 deaths to be observed and this would take about 30 years at our institution. This type of study would provide useful information for the Caribbean. We believe that it would be prudent to continue following this cohort of persons as well as enrolling new patients who are diagnosed with gastric cancer in order to better understand factors affecting survival in our population.

Of note, in this retrospective study we did not investigate the effect of chemotherapeutic interventions on survivorship. Numerous clinical trials have demonstrated the positive effect of such treatment on postoperative survival times of gastric cancer patients *vs* having just surgery[23].

Finally, modification of not only surgical but pathology staff practices may improve survivorship. Alteration of D2 gastrectomy to preserve pancreas and spleen has been shown to increase survival of stage three gastric cancer patients without any added risk of mortality or morbidity compared to D1 gastrectomy[24]. As previously mentioned, level of training of the pathology staff significantly affects the rate of retrieval of lymph nodes from surgical specimens. Education of relevant staff should be of benefit in that regard. Also, implementation of a surgical protocol ensuring AJCC recommendations, such as appropriate lymph node dissection, are followed, may improve specimen yield and thus diagnostic relevance. Epidemiological mapping of gastric cancer in the Afro-Caribbean population is of worldwide significance as, interestingly, relative rates of gastric cancer by ethnicity in England have been shown to be higher in black persons of Caribbean heritage[25].

COMMENTS

Background

Gastric adenocarcinoma is the most common type of cancer occurring the stomach. Despite robust clinical research, predominantly out of Japan, it remains a leading cause of cancer death both worldwide and in Jamaica. Before therapeutic strategies can be devised to reduce this burden in Jamaica, it is important to thoroughly describe both the pathological patterns seen here and the efficaciousness of current surgical management.

Research frontiers

D2 gastrectomy, especially as performed by well practiced experts, has been shown to improve patient survivorship. The role of adjuvant chemotherapy is gaining international acceptance as beneficial to survival following the MAGIC trial. The use of software, such as the Maruyama computer program, has shown reproducible and accurate retrospective prediction of lymph node involvement by level. This is a potential means of minimising perioperative morbidity and mortality, by obviating unnecessarily extensive lymph node dissection during gastrectomy.

Innovations and breakthroughs

In Asia, Europe and North America clinicopathological factors such as tumour size, lymph node metastases, vascular and serosal invasion have been demonstrated as significant factors affecting patient prognosis. In addition a trend has been noted of increased incidence of more proximal anatomic location of these tumours in the stomach. This study sought to see whether these findings were similar in a Caribbean population.

Applications

The findings of this study will be used to refine and standardise lymphadenectomy technique at the institution and in the region. This is the first study of its kind from the Caribbean region which differs significantly in racial composition, dietary practice and resource availability from the regions of origin of most published data.

Terminology

D1 gastrectomy–surgical resection of the stomach plus dissection of all group one or perigastric lymph nodes (left cardia, right cardia, lesser curve, greater curve, suprapyloric, infrapyloric); D2 gastrectomy–surgical resection of the stomach plus dissection of all perigastric lymph nodes plus those about the hepatic, left gastric, celiac, and splenic arteries, as well as those in the splenic hilum.

Peer review

It has been well written and presents the valid issues regarding association of various factors with the survival of gastric cancer patients.

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CLINICAL TRIALS STUDY

Laparoscopic re-sleeve gastrectomy as a treatment of weight regain after sleeve gastrectomy

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Abstract

AIM: To evaluate laparoscopic re-sleeve gastrectomy as a treatment of weight regain after Sleeve.

METHODS: Laparoscopic sleeve gastrectomy is a common bariatric procedure. Weight regain after long-term follow-up is reported. Patients were considered for laparoscopic re-sleeve gastrectomy when we observed progressive weight regain and persistence of comorbidities associated with evidence of dilated gastric fundus and/or antrum on upper gastro-intestinal series. Follow-up visits were scheduled at 1, 3, 6 and 12 mo after surgery and every 6 mo thereafter. Measures of change from baseline at different times were analyzed with the paired samples *t* test.

RESULTS: We observed progressive weight regain after sleeve in 11 of the 201 patients (5.4%) who had a mean follow-up of 21.1 ± 9.7 mo (range 6-57 mo). Three patients started to regain weight after 6 mo following Sleeve, 5 patients after 12 mo, 3 patients after 18 m. Re-sleeve gastrectomy was always performed by laparoscopy. The mean time of intervention was 55.8 ± 29.1 min. In all cases, neither intra-operative nor post-operative complications occurred. After 1 year follow-up we observed a significant ($P < 0.05$) mean body mass index reduction (-6.6 ± 2.7 kg/m^2) and mean % excess weight loss (%EWL) increase (+31.0% ± 15.8%). An important reduction of antihypertensive drugs and hypoglycemic agents was observed after re-sleeve in those patients affected by hypertension and diabetes. Joint problems and sleep apnea syndrome improved in all 11 patients.

CONCLUSION: Laparoscopic re-sleeve gastrectomy is a feasible and effective intervention to correct weight regain after sleeve.

Key words: Obesity; Bariatric surgery; Laparoscopic surgery; Stomach stapling; Gastrectomy; Surgery; Repeat

Core tip: Laparoscopic sleeve gastrectomy is gaining an important role in bariatric surgery because it may have similar results to gastric by-pass and duodenal switch, without problems of malabsorption and digestive anastomosis. However, weight regain after a long-term follow-up is reported. In this paper we show that re-sleeve gastrectomy is a valid and effective intervention to correct weight regain after sleeve.

Cesana G, Uccelli M, Ciccarese F, Carrieri D, Castello G, Olmi S. Laparoscopic re-sleeve gastrectomy as a treatment of weight regain after sleeve gastrectomy. *World J Gastrointest Surg* 2014; 6(6): 101-106 Available from: URL: http://www.wjgnet.com/1948-9366/full/v6/i6/101.htm DOI: http://dx.doi.org/10.4240/wjgs.v6.i6.101

INTRODUCTION

Laparoscopic sleeve gastrectomy (LSG) is a bariatric procedure that may allow similar results to Roux-en-Y gastric bypass (RYGB) and duodenal switch (DS), without problem of malabsorption[1-4]. Several studies, reporting large series, show that LSG is safe and effective in terms of weight loss[5-8] and improvement of comorbidities[9-11] in the first post-operative years. For these reasons and for the fact that it does not imply any digestive anastomosis, LSG has become very popular among surgeons. It appears that there are less complications after LSG compared to those seen after RYGB[7,12-14]. The most worrisome complication of LSG is a leak of the long suture line, reported in 1%-7% of patients[6]. Despite its wide diffusion, LSG's long-term weight loss data are not uniform. Some authors report a regain of weight after LSG[15-17]. This data could be in line with the fact that weight regain has been found after all bariatric operations[18,19]. One of the main advantages of LSG is that it may also work as a bridge procedure before a laparoscopic DS[20-22] or a laparoscopic RYGB[23], in case of insufficient weight loss or progressive weight regain. Recently, some authors suggested treating the inadequate weight loss, resulting from a large stomach or neofundus after LSG, with laparoscopic re-sleeve gastrectomy (LRSG)[24-27]. In this paper we present our series of 11 LRSG procedures with 1 year follow up.

MATERIALS AND METHODS

Patient characteristics

All patients who underwent LSG in our institution from December 2007 to September 2011 were considered for LRSG when we observed progressive weight regain and persistence of comorbidities, associated with evidence of persistence of gastric fundus and/or antrum on upper gastro-intestinal series (Figure 1B). No patients were considered for RYGB or DS after failed LSG because, in accordance with patients, we wanted to maintain the advantages of Sleeve in terms of avoiding post-operative malabsorption and in terms of preserving the possibility to easily explore the gastro-intestinal tract in the necessity of diagnostic or operative endoscopy. Institutional Review Board approval was obtained for the present study and all patients gave their informed consent prior to surgery. The presence of comorbidities, such as joint problems, was quantified according to anamnesis and use of specific medications before and after surgery. The presence of Diabetes was quantified by pre and post-operative fasting blood glucose (FBG) and glycosylated hemoglobin (HbA_{1c}). The presence of blood hypertension was quantified by systolic and diastolic pressure before and after surgery. The presence of sleep apnea was quantified by sleep studies before surgery and post-operative resolution by discontinuation of the use of CPAP (Continuous Positive Airway Pressure) mask.

Surgical technique

Surgery was performed according to our usual technique for laparoscopic Sleeve Gastrectomy. A Veress needle was used to accomplish pneumoperitoneum. The first trocar (12 mm, Endopath XCEL, Ethicon Endo-surgery, Cincinnati, OH, United States) was placed in the left subcostal space. The second and the third trocars (5 mm, Endopath XCEL, Ethicon Endo-surgery, Cincinnati, OH, United States) were placed in the subxiphoid space and in the right flank respectively. The last trocar (15 mm, Endopath XCEL, Ethicon Endo-surgery, Cincinnati, OH, United States) was placed above the umbilicus. The stomach was separated from the gastrocolic ligament and gastrosplenic ligament by Harmonic ACE 5 mm (Ethicon Endo-Surgery, Cincinnati, OH, United States). The left diaphragmatic crus was freed. The excessive part of the stomach was cut over a 12.7 mm (38 Fr) Gastric Calibration Tube (Ethicon Endo-Surgery, Cincinnati, OH, United States) starting from 6 cm proximal to the pylorus and proceeding up toward the diaphragmatic left crus. An articulating endoscopic linear cutter (Echelon Flex 60, Ethicon Endo-Surgery, Cincinnati, OHIO, United States) with 4.1 mm (Green) and 3.8 mm (Gold), 6 row cartridges (Endoscopic Linear Cutter Reloads, Ethicon Endosurgery, Cincinnati, OH, United States), was used to staple the stomach. In LRSG we rarely used 3.5 mm (Blue) cartridges because of the tissue's density after the prior stapling. Running suture with PDS 3/0 (MIC55E, PDS* Ⅱ, Ethicon Endo-Clip Suture, Cincinnati, OH, United States) was used to reinforce the stapled line. Surgical technique was the same in LSG and LRSG. The same calibration tube was used for all the patients in LSG and LRSG.

Post-operative management

Patients were started on an oral fluid diet on post-operative day 3 after upper gastro-intestinal series had shown no leak. Patients were discharged on day 5 if no post-operative complications occurred. Follow-up visits were scheduled at 1, 3, 6 and 12 mo after surgery and every 6 mo thereafter. Data were entered into a prospectively held database including age, gender, body mass index (BMI), excess of weight (EW), % of excess weight loss (%EWL), comorbidities before and after surgery, post-operative complications.

Statistical analysis

Data were obtained by review of the prospectively maintained database. Quantitative variables were reported as mean and standard deviation (SD); qualitative variables were described as number and percentages. Measures of change from baseline at 3, 6, 12 mo after surgery were analyzed with the paired *t* test. Statistical significance was set at $P \leqslant 0.05$. All statistical analyses were performed with the Statistical Product and Service Solutions (SPSS) software package (version 19, SPSS-IBM, Chicago, IL, United States).

RESULTS

Patients characteristics

From December 2007 to September 2011, 201 patients

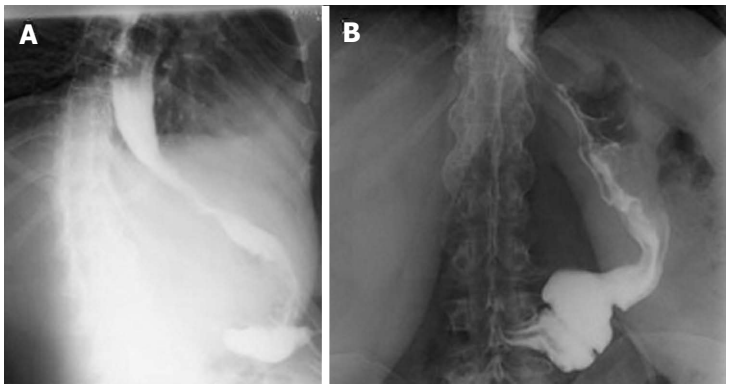

Figure 1 Comparison of upper gastro-intestinal series in the same patient on post-operative day 2 after sleeve gastrectomy (A) and one year later (B). After one year we see a dilated stomach (B) that allows weight regain.

Table 1 Pre-operative patients' characteristics *n* (%)

Characteristics	Value, mean ± SD *n* = 11
Age (yr)	40.6 ± 10.2
Height (m)	1.60 ± 0.1
Ideal body weight (kg)	57.4 ± 8.9
Excess body weight (kg)	59.3 ± 16
Excess body weight (%)	104.2 ± 25.5
Body mass index (kg/m^2)	45.2 ± 5.6
Gender	
Male	3 (27.3)
Female	8 (72.7)
Comorbidities	
At least 1 comorbidity	4 (36.4)
Blood hypertension	3 (27.3)
Type 2 diabetes mellitus	2 (18.2)
Sleep apnea syndrome	1 (9.1)
Joint problems	3 (27.3)

underwent LSG at our Institution. We observed progressive weight regain in 11 patients (5.4%). Three patients started to regain weight after 6 mo post-LSG, 5 patients after 12 mo, 3 patients after 18 mo. An upper gastro-intestinal series showed gastric dilatation in all 11 patients. Three patients (27.3%) had another bariatric surgery prior to LSG: 2 patients had an adjustable gastric band (AGB) already removed before LSG and one patient underwent surgical intervention of laparoscopic Band removal and LSG at the same time. The AGB was removed because of dysfunction associated with weight regain.

Four patients (45.5%) were affected by at least 1 comorbidity (Table 1). Two of them (a female with BMI = 54.1 kg/m^2 and a male with BMI = 48.5 kg/m^2) were affected by blood hypertension, type II diabetes and joint problems. A third patient, a female with BMI = 52.7 kg/m^2, was affected by blood hypertension and joint problems. A fourth patient, a male with BMI = 43.3 kg/m^2, was affected by sleep apnea syndrome. In all patients, pre-operative blood hypertension was well controlled by drugs (mean systolic 123.3 ± 2.9 mmHg and mean diastolic 78.3 ± 2.9 mmHg). Two patients were in therapy with combination diuretics and ACE inhibitors; one patients with ACE inhibitors alone. Regarding the treatment of diabetes, the two patients affected used oral hypoglycemic agents. The average FBG before surgery was 147.5 ± 3.5 mg/dL and HbA$_{1c}$ averaged 6.9% ± 0.1%. The mean age of the patients (3 males and 8 females) was 40.6 ± 10.2 years (Table 1).

Findings after LSG

Before LSG, mean absolute weight was 116.4 ± 21.5 kg, mean EW was 59.3 ± 16 kg and mean BMI was 45.2 ± 5.6 kg/m^2 (Table 1). One patient developed a high gastric leak after LSG and underwent a second operation six days later. She was a female with BMI = 41 kg/m^2 and no comorbidities. She had surgical revision of the gastric staple line without resewing it. A perigastric abscess was drained and a drain tube was left in place. The leak resolved in 15 d and the patient was discharged on day 18. BMI and %EWL variations after LSG are collected in Figure 2. After an initial decrease, mean BMI start to increase after 6 mo.

After LSG, systolic and diastolic pressure values did not differ significantly to prior LSG; however a reduction in requirement of antihypertensive drugs was observed. One patient suspended therapy and the others 2 reduced therapy. After LSG, FBG and HbA$_{1c}$ showed an important decrease (respectively 105.5 ± 28.9 mg/dL and 6.2% ± 0.5%). One of two patients (50%) suspended oral hypoglycemic agents. Joint problems and sleep apnea syndrome improved in all (100%).

Findings after LRSG

LRSG was performed at a mean interval of 21.1 ± 9.7 mo after LSG. The mean BMI before LRSG was 38.9 ± 3.8 kg/m^2 and the mean %EWL was 25.3% ± 14.2% (Figure 2). LRSG was completed laparoscopically in all cases and no intra-operative or post-operative complications occurred. The mean time of intervention was 55.8 ± 29.1 min. The mean operative time for LSG in the same patients was longer: 65.4 ± 17.4 min. This finding could be related to the fact that when we perform LRSG the stomach is already dissected and prepared. We only cut off the exceeding part of the stomach over the boogie. No significative blood loss occurred either in LSG or in LRSG. No patient showed leakage from the stapled line at upper gastro-intestinal series scheduled on day 2. All patients resumed an oral liquid diet on day 3 and they were discharged from the hospital on day 5 after LRSG. At 1, 6, 12 mo after LRSG the BMI progressively decreased and %EWL increased in each patient. As shown

Table 2 Weight loss at 12 mo after laparoscopic re-sleeve gastrectomy

	Value (n = 11) before LRSG mean ± SD	After LRSG mean ± SD	Mean change (SD)	95%CI	P value
Absolute weight (kg)	100.3 ± 17.5	82.9 ± 14.7	-17.4 (± 7.8)	-12.0--22.6	< 0.001
BMI (kg/m^2)	38.9 ± 3.8	32.2 ± 3.9	-6.6 (± 2.7)	-4.8--8.5	< 0.001
Excess weight (kg)	43.2 ± 10.1	25.8 ± 9.5	-17.4 (± 7.8)	-12.0--22.6	< 0.001
Excess weight (%)	75.4 ± 11.6	45.4 ± 16.5	-29.2 (± 12.4)	-20.8--37.6	< 0.001
Excess weight loss (%)	25.3 ± 14.2	56.8 ± 12.4	+31.0 (± 15.8)	41.6-20.4	< 0.001

P value is calculated with paired t test assessing change from LRSG. BMI: Body mass index; LRSG: Laparoscopic re-sleeve gastrectomy.

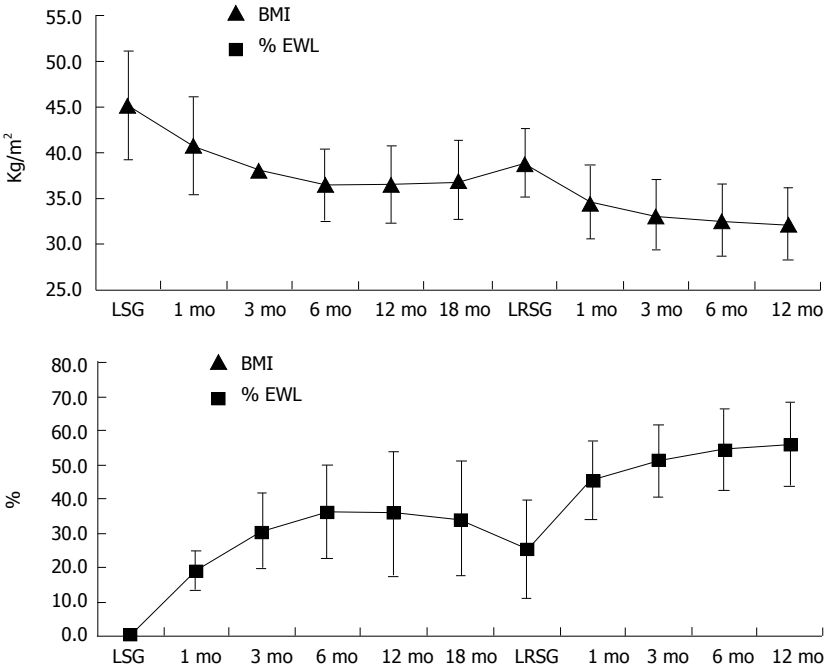

Figure 2 Body mass index and % of excess weight loss before and after laparoscopic sleeve gastrectomy and laparoscopic re-sleeve gastrectomy. Data are expressed as means and standard deviations. BMI decrease and %EWL increases for few months (mo) after LSG, then patients start to regain weight. After LRSG, BMI decreases and %EWL increases again. BMI: Body mass index; %EWL: % of excess weight loss; LSG: Laparoscopic sleeve gastrectomy; LRSG: Laparoscopic re-sleeve gastrectomy.

in Table 2, after 1 year of follow-up the mean BMI significantly decreased from 38.9 ± 3.4 kg/m^2 to 32.2 ± 3.9 kg/m^2 (P < 0.05) and the %EWL significantly increased from 25.3 ± 14.2 to 56.3 ± 12.4 (P < 0.05).

After LRSG only 1 of 3 patients continued to use antihypertensive drugs and only 1 of 2 continued to use oral hypoglycemic agents. Mean systolic pressure was 121.6 ± 1.5 mmHg and mean diastolic was 78 ± 2 mmHg. Mean FBG was 98.5 ± 16.2 mg/dL and mean HbA_{1c} was 6.1 ± 0.6 %. Neither joint problems nor sleep apnea were noted after LRSG.

DISCUSSION

LSG is gaining an important role in bariatric surgery because it may have similar results to RYGB and DS, without malabsorbitive problems and digestive anastomosis[1-3]. Moreover, after LSG there are no problems exploring the upper gastro-intestinal tract. Some authors have noted a weight regain after LSG[15-17]. In our series we observed weight regain in 11 out of 201 patients (5.4%), who had a mean follow-up of 21.1 ± 9.7 mo (range 6-57 mo). Three patients started to regain weight after 6 mo post-LSG, 5 patients after 12 mo, 3 patients after 18 mo. An upper gastro-intestinal series was performed and showed a dilatation of the antrum and/or gastric fundus in all the 11 patients (Figure 1). The causes of gastric dilatation are not clear[27]. It could be related to a technical problem or to a natural process of stomach tissue dilatation. The main technical cause for a dilated antrum might be a dissection started farther than 6 cm from the pylorus. In these cases the patients will regain weight after a few months. The main cause for a dilated fundus might be a dissection farther than 1 cm to the left of the esophagus. A complete dissection of the gastric fundus is difficult when the patient underwent prior AGB placement or removal. Other causes of stomach tissue dilatation after LSG, besides technical problems, could be related to patient's psychological problems or negligence in following the post-surgical diet recommendations. We believe that these factors, technical and not, are often both involved in the process of weight regain after LSG. For example, an incomplete section of the gastric fundus will not decrease the secretion of ghrelin[27], which can explain the incapacity of the patient to follow diet recommendations, therefore permitting stomach dilatation and weight regain.

In order to resume weight loss in patients for which LSG failed, there are few surgical options. LSG can be converted to RYGB or DS[20-23], or a LRSG can be performed[24-27]. In our series, no patients underwent RYGB

or DS because we wanted to maintain the advantages of LSG in terms of avoiding malabsorption or gastro-intestinal anastomosis, and of preserving the possibility to easily explore the gastro-intestinal tract in the necessity of diagnostic or operative endoscopy. Our patients underwent LRSG over the same calibration tube of LSG: 12.7 cm boogie (38 Fr). After LSG, the gastric tissue around the stapled line is denser because of the scar' s healing and remodeling. For this reason, we used only Green (4.1 mm) and Gold (3.8 mm) cartridges to dissect the stomach in the LRSG. An oversewing suture of the stapled line was always performed.

LRSG was feasible in all patients in our series. Although we had neither intra-operative nor post-operative complications, the main post-operative problem after LRSG may be the same of LSG: leakage from the long stapled line. LRSG was effective for weight loss in all patients (Table 2). After one year follow-up we noted a significant decrease in mean BMI from 38.9 ± 3.4 kg/m^2 to 32.2 ± 3.9 kg/m^2 ($P < 0.05$) and a significant increase in mean %EWL from 25.3 ± 14.2 to 56.3 ± 12.4 ($P < 0.05$) (Figure 2). Although median BMI was > 30 kg/m^2 after one year, we noted a significative trend in decreasing weight after LRSG. We need a longer follow-up to determine if the treatment is really effective, but these preliminary data are encouraging in not substituting LSG with a malabsorbitive intervention, loosing the advantages of LSG, especially in terms of quality of life. If weight regain will still occur after a longer follow-up post-LRSG, patients will undergo upper gastro-intestinal series. If the series will show a dilatation of the stomach, the patient will undergo another LRSG. If patients will regain weight without signs of stomach dilatation, he will be led to a malabsorbitive intervention.

Comorbidities improved: sleep apneas and joint problems disappeared completely 12 mo after LSG. Blood hypertension values did not differ significantly before surgery, after LSG and after LRSG, but a significant reduction in the requirement of antihypertensive drugs was observed. FBG and HbA_{1c} gradually decreased after LSG and LRSG. One of two patient suspended oral hypoglycemic agents.

In conclusion, like the other major bariatric interventions[18,19] LSG can result in weight regain. Other bariatric procedures can be performed to correct it[20-27]. In our series of patients who regained weight after LSG, LRSG was performed. The result was a safe procedure which allowed a significant weight loss in each patient. LRSG appears to be a valid correction for post-LSG weight regain. Our study is limited by the fact that it is retrospective, involves few patients and has a limited follow-up (12 mo after LRSG). We believe that these preliminary data can be a promising start for further studies, which are needed to confirm the initial results.

COMMENTS

Background

Obesity is an increasing problem in modern western society. In the past few years, different types of surgery have been developed to resolve this problem when it could not be treated by diets or drugs. Sleeve gastrectomy is an intervention that allows for good results in term of weight loss without problems of malabsorption. Sleeve became very popular among surgeons. Despite its wide diffusion, sleeve's long-term weight loss data are not uniform. Some authors report a regain of weight after Sleeve.

Research frontiers

To show that it is feasible and effective to correct weight regain after sleeve through a re-sleeve gastrectomy.

Innovations and breakthroughs

Re-sleeve gastrectomy can correct weight regain after sleeve. It avoids converting sleeve in a malabsorbitive intervention, loosing the advantages of sleeve. They describe the surgical technique, which is valid and without major complications.

Applications

Sleeve gastrectomy has advantages in terms of quality of life for obese patients, avoiding problems of malabsorption and allowing weight lost. The possibility of managing weight regain with a re-sleeve, without converting it in a malabsorbitive intervention, can allow surgeons to choose this type of surgery in the cure of obesity.

Terminology

Sleeve gastrectomy is a vertical resection of stomach. Re-sleeve gastrectomy is the resection of those parts of stomach that underwent dilatation after sleeve.

Peer review

This is a case series of laparoscopic re-sleeve gastrectomy in obese patients who showed weight regain after laparoscopic sleeve gastrectomy. The present study is important because there are few data on this type of bariatric surgery.

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CASE REPORT

Downstaging and resection after neoadjuvant therapy for fibrolamellar hepatocellular carcinoma

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Abstract

Fibrolamellar hepatocellular carcinoma (FLHCC) is a rare malignant liver neoplasm, commonly observed in adolescents and young adults of both genders. The disease is more common in Caucasians and in patients without a prior history of liver disease. The best treatment option is a surgical resection associated with liver hilum lymph node dissection. However, there is no established systemic drug treatment for patients with locally advanced or metastatic disease. We report on a patient with advanced FLHCC, initially considered unresectable due to invasion of the right and the middle hepatic veins and circumferential involvement of the left hepatic vein. Following the treatment with gemcitabine-oxaliplatin systemic chemotherapy, the patient exhibited a significant tumor reduction. As a result, a complete resection was performed with an extended right hepatectomy associated with a partial resection of the inferior vena cava, a wedge resection in segment 2, and lymphadenectomy of the hepatic hilum. The case was unusual due to the significant tumor downstaging with gemcitabine-oxaliplatin, potentially enabling curative resection. More studies are needed to confirm the efficacy of the systemic drug treatment for FLHCC.

Key words: Chemotherapy; Gemcitabine; Oxaliplatin; Hepatectomy; Hepatic veins; Fibrolamellar hepatocellular carcinoma

Core tip: Fibrolamellar hepatocellular carcinoma (FLHCC) is a rare malignant liver neoplasm. The best treatment option is a surgical resection with liver hilum lymph node dissection. Currently there is no established systemic drug treatment for patients with locally advanced or metastatic disease. In this report, a patient with advanced FLHCC, initially considered unresectable due to vascular invasion, exhibited a significant tumor reduction following systemic chemotherapy with gemcitabine-oxaliplatin, allowing resection. This was an unusual case where gemcitabine-oxaliplatin treatment led to a significant tumor downstaging enabling curative resection. Additional studies are needed to confirm the efficacy of the systemic drug treatment for FLHCC.

Fonseca GM, Varella AD, Coelho FF, Abe ES, Dumarco RB, Herman P. Downstaging and resection after neoadjuvant therapy for fibrolamellar hepatocellular carcinoma. *World J Gastrointest Surg* 2014; 6(6): 107-111 Available from: URL: http://www.wjgnet.com/1948-9366/full/v6/i6/107.htm DOI: http://dx.doi.org/10.4240/wjgs.v6.i6.107

INTRODUCTION

Fibrolamellar hepatocellular carcinoma (FLHCC) is

an uncommon primary liver neoplasm, representing 0.6%-8.6% of all hepatocellular carcinomas (HCC)[1]. It was first described in 1956 by Edmonson as a rare distinctive form of HCC[2]. In general, it is a vascular tumor with prominent fibrosis. Microscopically, FLHCC appears as a well-differentiated tumor comprised of large polygonal cells with large nuclei and nucleoli, as well as an abundant eosinophilic cytoplasm, arranged in lamellar bands of collagen fibers[3]. FLHCC most often affects adolescents and young adults of both genders, often Caucasian, and without a prior history of liver disease[1,4]. Liver function tests are typically normal or only mildly elevated. Commonly used HCC markers, such as alpha-fetoprotein, are of little help in diagnosing and monitoring disease progression in the majority of patients, as only a small proportion of patients (7%-11%) show elevation in alpha-fetoprotein levels[5,6].

FLHCC is believed to more commonly metastasize to regional lymph nodes. The cornerstone for FLHCC treatment is a surgical resection associated with lymph node dissection[3,4]. Patients with advanced FLHCC represent a population in need of novel and effective treatments. Due to the lack of data on effective systemic drug treatments as well as the FLHCC patients' paucity, it is difficult to conduct clinical trials[1]. The authors report an unusual case of a young patient, initially with an unresectable FLHCC, treated with gemcitabine-oxaliplatin (GEMOX), resulting in an excellent response and complete resection of the tumor.

CASE REPORT

A previously healthy 35-year-old Caucasian female complaining of abdominal pain, 3 kg weight loss, weakness, back pain, and a palpable mass in the right upper quadrant, was referred for evaluation. Physical examination disclosed a palpable hard mass 20 cm below the right costal margin. There were no signs of liver disease or other relevant findings. A computed tomography scan (Figure 1) showed a suggestive FLHCC mass (17 cm × 15 cm) affecting the right liver lobe. In addition, the mass affected segment 4b by obstructing the right portal branch, invading both the right and middle hepatic veins, circumferentially wrapping the left hepatic vein, and compressing the inferior vena cava. A lesion (ø 6.5 cm) in segment 2 displayed the same characteristics, as well as lymphadenopathy at the liver hilum up to 2.7 cm in size. Laboratory tests revealed elevated levels of alkaline phosphatase, gamma-glutamyl transpeptidase, and alpha-fetoprotein (44.395 ng/mL). Both hepatitis B and C serologies were negative. Colonoscopy and endoscopy results were normal. Percutaneous biopsy of the tumor confirmed FLHCC. The lesion was considered unresectable because of the extensive vascular involvement, especially of the hepatic veins; therefore, the patient was referred to an oncologist for a systemic drug treatment. Transplantation was eliminated due to the presence of the hilar lymph nodes (extra hepatic disease).

The patient received 100 mg of oxaliplatin and 1400 mg of gemcitabine (20 mg/kg) every two weeks during an 11-mo treatment period, with good tolerance. The staging intervals, scheduled every four months, included either a computed tomography scan or magnetic resonance imaging. After one year of treatment, magnetic resonance imaging showed significant tumor size reduction (the larger lesion size was 8.5 cm and the smaller 2.2 cm), decrease in contact with the left hepatic vein and inferior vena cava, disappearance of the lymphadenopathy, and hypertrophy of the left lateral segment of the liver (38% of total liver volume) (Figure 1). In addition, there was a significant decrease in alpha-fetoprotein levels to 45 ng/mL.

The patient was submitted to an extended right hepatectomy with partial resection of the inferior vena cava associated with a wedge resection in segment 2 and lymphadenectomy of the hepatic hilum. The procedure lasted 450 min with the patient receiving two units of packed red blood cells and staying in the intensive care unit for two days. The patient developed a postoperative biliary fistula, which was treated conservatively, with spontaneous closure after 28 d. Our patient was discharged on the 17th postoperative day in a good clinical condition.

Histology examination confirmed FLHCC with microscopically free margins (R0 resection). The hepatic hilum lymph nodes were free of the disease. At discharge, the level of alpha-fetoprotein was within normal limits (4.7 ng/mL). The patient had no signs of the disease recurrence at the 14-mo follow-up.

DISCUSSION

The best treatment option for FLHCC is a resection with adequate lymph node dissection[3,5]. However, a resection is not always possible due to locally advanced disease. The best therapy for these patients has not been well established[1]. Several chemotherapy agents have been used for FLHCC treatment, including fluoropyrimidines, doxorubicin, cisplatin, oxaliplatin, gemcitabine, and irinotecan, as well as interferon, bevacizumab, and sorafenib in either combination regimens or separately[1,5]. Locoregional therapies, such as transarterial chemoembolization, radiofrequency ablation, external beam radiation, percutaneous ethanol injection, and hepatic arterial infusion of cisplatin, had disappointing results[1,5]. A study from the Fibrolamellar Carcinoma Consortium, which contained 99 patients diagnosed with FLHCC, showed that from the 73 patients who underwent surgery, 13% (10/73) received preoperative chemotherapy, external beam radiation, and/or transarterial chemoembolization. Twenty one percent (20/99) were considered to have unresectable disease and 13 of them were treated with various combinations of systemic drug therapy with or without locoregional therapies. Chemotherapy agents used in the study included fluoropyrimidines, doxorubicin, cisplatin, oxaliplatin, gemcitabine, and irinotecan. However, a multivariate analysis showed a lack of surgery to be an independently poor overall survival predictor[1]. Kaseb *et al*[7] studied 94 FLHCC patients and found tumor resection

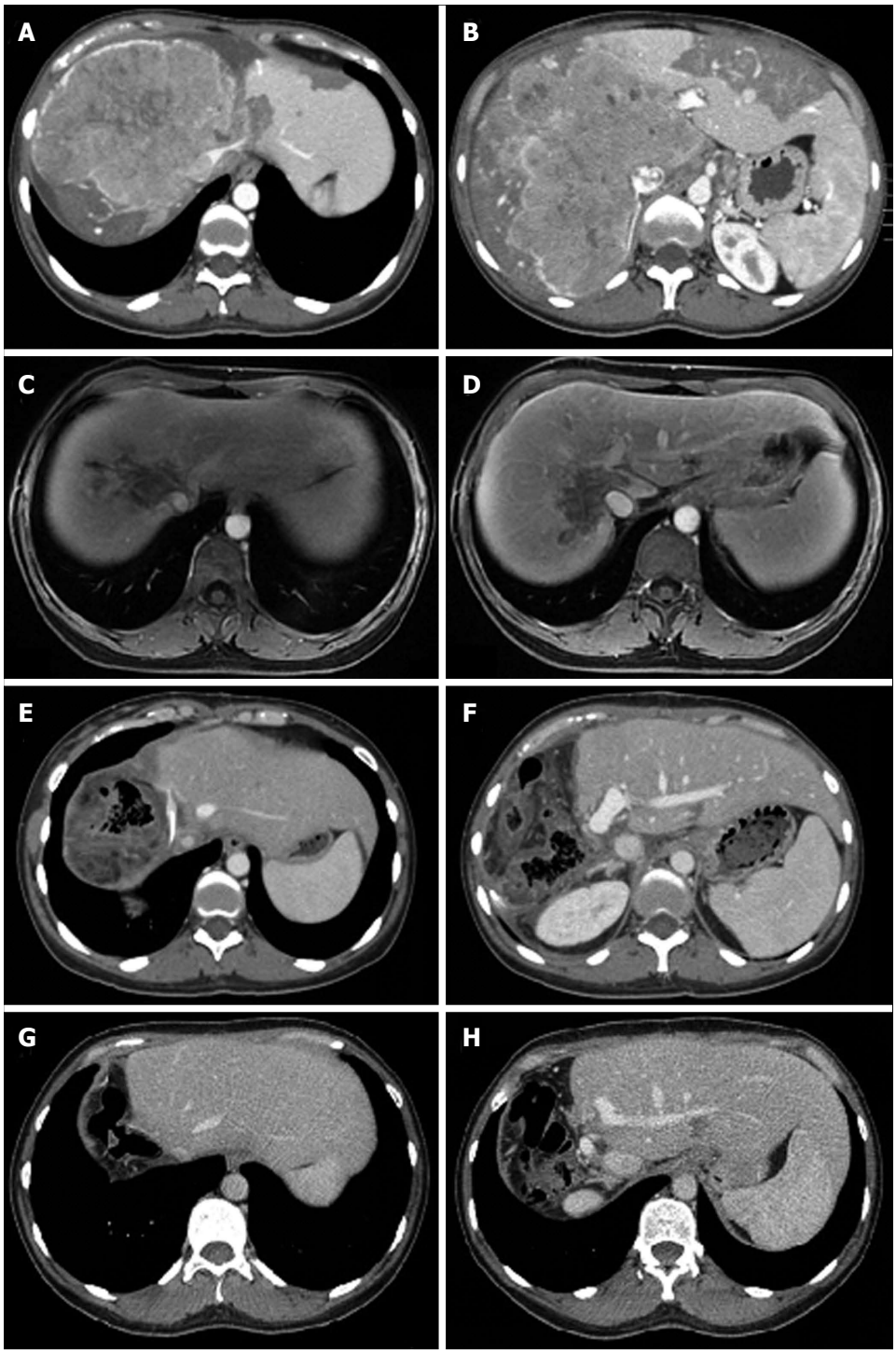

Figure 1 Abdominal computed tomography and magnetic resonance imaging of a 35-year-old Caucasian female, with no previous history of liver disease, showing a large mass in the upper right quadrant. A, B: Abdominal computed tomography (CT) before chemotherapy showing a large mass invading (17 cm × 15 cm) the right and the middle hepatic veins, and surrounding the left hepatic vein; C, D: Abdominal magnetic resonance imaging after gemcitabine-oxaliplatin chemotherapy showing significant reduction of the tumor size; E, F: Abdominal CT two weeks after surgery with hypertrophy of the left lateral segment of liver (liver remnant), and free and patent left branch of the portal vein and left hepatic vein; G, H: Late follow-up after 14 mo.

to be a factor positively associated with longer overall survival; 5-fluorouracil-interferon combination was the most frequently used systemic therapy.

HCC markers, such as alpha-fetoprotein, are of little help in diagnosing and monitoring disease progression in the majority of patients. This is mostly due to a small proportion of patients (7%-11%) showing elevated alpha-fetoprotein levels[5,6]. Our patient probably belongs to this peculiar group since her initial levels of alpha-fetoprotein were high, and were lowered to normal levels following surgery.

Sorafenib is currently the standard treatment for advanced HCC[8,9]. However, no systemic drug therapy had convincingly improved survival among patients with

advanced HCC. There have been attempts to evaluate the efficacy of new drugs or combination treatments in clinical trials. Some of the examples of these trials include: (1) doxorubicin alone and/or with gemcitabine; (2) combination of cisplatin, doxorubicin, 5-fluorouracil, and alpha-interferon; and (3) combination of irinotecan, taxanes, gemcitabine, topotecan, and thymidilate synthase inhibitors[10]. The GEMOX regimen appeared to be the most promising, based on a lack of renal and hepatic toxicity in cirrhotic patients, promising efficacy in the phase II trials for advanced HCC, and with possible extended benefit for Child B cirrhosis[10-13]. Louafi *et al*[12], studying 32 patients treated for advanced HCC, had two patients that underwent HCC curative resection after partial response to GEMOX. In a retrospective multicenter study, Zaanan *et al*[10] observed tumor responses in 204 patients with advanced HCC treated with GEMOX. In 10 patients, tumor response either permitted secondary surgical resection of residual tumors or orthotopic liver transplantation. Radiofrequency ablation was performed in one patient, transcatheter arterial chemoembolization in three patients, cyberknife treatment in one patient, and radioembolization in two patients. There was also a case report on a patient with metastatic HCC without liver disease with a complete response after 12 cycles of GEMOX[14].

There has been only one reported case of FLHCC with a complete response after GEMOX treatment. In this case, a young woman had a histologically proven metastatic lymph node relapse after resection of the primary tumor. GEMOX regimen lead to a complete response without relapse five years after chemotherapy discontinuation[15].

HCC patients have poor tolerance to systemic chemotherapy, mostly due to cirrhotic liver[15]. In most cases FLHCC patients do not have a prior history of liver disease[4]. This may explain the better tolerance to chemotherapy, hence leading to a better response, as is the case in our patient. In the present case, the chemotherapy regimen with GEMOX promoted FLHCC downstaging, potentially allowing for a curative treatment. However, more studies are needed to confirm GEMOX efficacy.

COMMENTS

Case characteristics

A previously healthy 35-year-old Caucasian female complained of abdominal pain, 3 kg weight loss, weakness, back pain, and a palpable mass in the right upper quadrant.

Clinical diagnosis

A palpable hard mass was found to be located 20 cm below the right costal margin with no signs of liver disease.

Differential diagnosis

Hepatocellular carcinoma, cholangiocarcinoma, liver metastasis.

Laboratory diagnosis

The patient had elevated levels of alkaline phosphatase, gamma-glutamyl transpeptidase, and alpha-fetoprotein, and negative serologies for both hepatitis B and C.

Imaging diagnosis

A computed tomography scan showed a suggestive fibrolamellar hepatocellular carcinoma (FLHCC) mass (17 cm × 15 cm) affecting the right liver lobe and segment 4b, obstructing the right portal branch, invading the right and middle hepatic veins, circumferentially wrapping the left hepatic vein, and compressing the inferior vena cava; the second lesion (6.5 cm) in segment 2 had the same characteristics and lymphadenopathy at the liver hilum (up to 2.7 cm), with colonoscopy and endoscopy results being normal.

Pathological diagnosis

FLHCC was confirmed by percutaneous biopsy of the tumor.

Treatment

The patient received 1400 mg of gemcitabine (20 mg/kg) and 100 mg of oxaliplatin (GEMOX) every 2 wk over 11 mo, with a significant tumor reduction, allowing for resection.

Related reports

The best treatment option for FLHCC is resection with adequate lymph node dissection. However, resection is not always possible due to local disease advancement. There has not been well-established disease therapy for these patients.

Term explanation

FLHCC is an uncommon primary liver neoplasm. In general, it is a vascular tumor with prominent fibrosis. Microscopically, FLHCC appears as a well-differentiated tumor comprised of large polygonal cells with large nuclei and nucleoli, as well as an abundant eosinophilic cytoplasm, arranged in lamellar bands of collagen fibers.

Experiences and lessons

In the present case, the chemotherapy regimen with GEMOX promoted FLHCC downstaging, potentially allowing for curative treatment and suggesting GEMOX as a possible chemotherapy treatment for patients with advanced FLHCC; however, more studies are needed to confirm GEMOX efficacy.

Peer review

This is an interesting case of a young female with an initially considered unresectable FLHCC. Significant tumor downstaging with GEMOX allowed surgical resection.

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CASE REPORT

Intra-abdominal esophageal duplication cyst: A case report and review of the literature

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Abstract

Intra-abdominal esophageal duplications are rare entities in adults. They are mostly asymptomatic, but since they can lead to complications surgical excision is advised for all duplication cysts. We present a case of a 20-year-old male with colic-like abdominal pain, mimicking symptoms of cholecystolithiasis. However after cholecystectomy the symptoms were still present. A computed tomography-scan of the abdomen and an endoscopic ultrasound revealed a cyst of the esophagus of 3.0 cm × 2.3 cm in size. Diagnostic laparoscopy was planned, during which we observed a para-esophageal cyst at the gastro-esophageal junction. Laparoscopic excision of this cyst was performed. Pathophysiological examination revealed an esophageal duplication cyst. We report a rare case of a symptomatic intra-abdominal esophageal duplication cyst in an adult. One must consider this diagnosis when more common diagnoses to account for the patient's symptoms are excluded. Removal of duplication cysts can be done laparoscopically.

Key words: Esophageal duplication cyst; Intra-abdominal; Symptomatic; Laparoscopy

Core tip: Intra-abdominal esophageal duplication cysts are rare entities in adults, especially when they are symptomatic. Since these anomalies can lead to complications surgical excision is advised for all of them. We present a case of a 20-year-old male with colic-like abdominal pain, mimicking symptoms of cholecystolithiasis, but caused by an intra-abdominal duplication cyst of the esophagus. The cyst was excised laparoscopically. The procedure was uneventful and the patient was free of symptoms. This case shows that one must consider the diagnosis of a symptomatic intra-abdominal esophageal duplication cyst when more common diagnoses to account for the patient's symptoms are excluded.

Castelijns PSS, Woensdregt K, Hoevenaars B, Nieuwenhuijzen GAP. Intra-abdominal esophageal duplication cyst: A case report and review of the literature. *World J Gastrointest Surg* 2014; 6(6): 112-116 Available from: URL: http://www.wjgnet.com/1948-9366/full/v6/i6/112.htm DOI: http://dx.doi.org/10.4240/wjgs.v6.i6.112

INTRODUCTION

Gastroenteric duplication cysts are congenital malformations that may affect the gastro-intestinal tract from mouth to anus. They are usually attached to the gastrointestinal tract, have smooth muscle cells in the wall of the cyst and are lined with gastrointestinal epithelium. Most of them are found in the small intestine (44%), the esophagus (20%) or in the large intestine (15%)[1]. Esophageal duplication cysts mostly arise in the mediastinum.

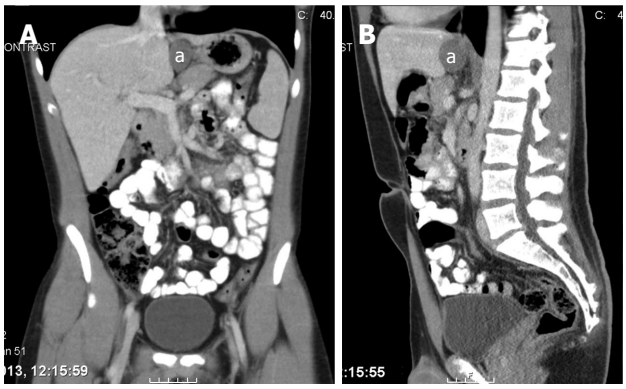

Figure 1 Computed tomography images of the esophageal duplication cyst (a). A: Frontal view; B: Sagittal view.

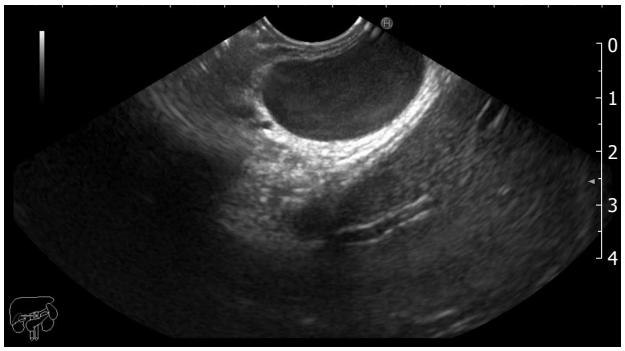

Figure 2 Endoscopic ultrasound image of the cyst.

There are only a few case reports that describe intra-abdominal esophageal duplication.

Duplication cysts may be symptomatic, but even then definitive pre-operative diagnosis can be difficult because of non-specific clinical symptoms. Also, symptoms might be mistaken for other more common abdominal conditions. Because of potential complications such as bleeding, infection or conversion to a malignancy, currently the most common treatment of these anomalies is surgical excision, even if they are not symptomatic.

CASE REPORT

We present a 20-year-old male with no medical or surgical history who was evaluated because of nausea and recurrent colic pain in the right upper abdomen radiating towards his back, but no vomiting or fever. Ultrasound of the upper abdomen was performed, which showed gallstones but no other abnormalities. Initially, symptomatic cholecystolithiasis was considered as the primary diagnosis and subsequently our patient underwent a laparoscopic cholecystectomy. The procedure was performed without complications and the patient was initially free from symptoms.

However, one year later he presented again with the same symptoms as before. Physical examination and laboratory testing did not reveal any abnormalities. The differential diagnosis at this point was choledocholithiasis or urolithiasis. Ultrasound of the abdomen showed no dilatation of intra- or extrahepatic bile ducts or choledocholithiasis. A computed tomography (CT)-scan of the abdomen revealed no urolithiasis, but it did show a mass at the gastro-esophageal junction that was further evaluated with endoscopic ultrasonography (EUS). EUS identified a 3.2 cm × 2.8 cm sized smooth lined lesion (Figure 1) in the distal esophagus just below the diaphragm (Figure 2) We could not differentiate between a gastrointestinal cyst or a leiomyoma, necessitating further analysis.

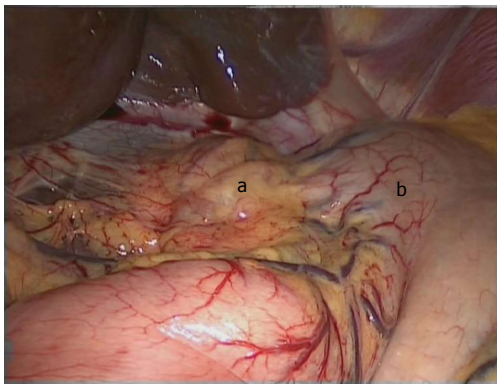

Figure 3 Preoperative image with the cyst (a) medial to the esophagus and stomach (b).

Endoscopic fine needle aspiration revealed mucinous material without any signs of malignant cells on histopathological examination. Gastro-intestinal duplication cyst was considered as one of the possible diagnoses and diagnostic laparoscopy was planned. During laparoscopic exploration we observed a 3 cm × 3 cm sized paraesophageal cystic lesion at the gastro-esophageal junction, 2-3 cm above the Z-line (Figure 3). The cyst was dissected free and the connection with the oesophagus was excised with an endoGIA© after which the staple line was oversewn with a V-loc© suture. The procedure went uneventful.

Histopathological analysis of the specimen revealed a 30 mm × 30 mm × 25 mm sized cyst filled with clear fluid. The wall had a thickness of 3 mm and consisted of two muscular layers lined by respiratory columnar epithelium without any signs of cartilage tissue found in the cyst (typical for bronchogenic cysts) and therefore the final diagnosis of esophageal duplication cyst was suggested (Figure 4).

The postoperative course was uncomplicated and the patient could be discharged on day two postoperatively. At follow up 5 mo later the patient did not display any of the earlier experienced abdominal symptoms.

DISCUSSION

Gastrointestinal duplication cysts are very rare abnormalities. Autopsy studies have shown a prevalence of approximately 1:4500 and esophageal duplications occur even less frequently, 1:8200[2,3]. Only a few cases are described in which the cyst is connected to the intra-abdominal part of the esophagus. Only ten percent of the esophageal cysts communicate with the lumen of the esophagus[4].

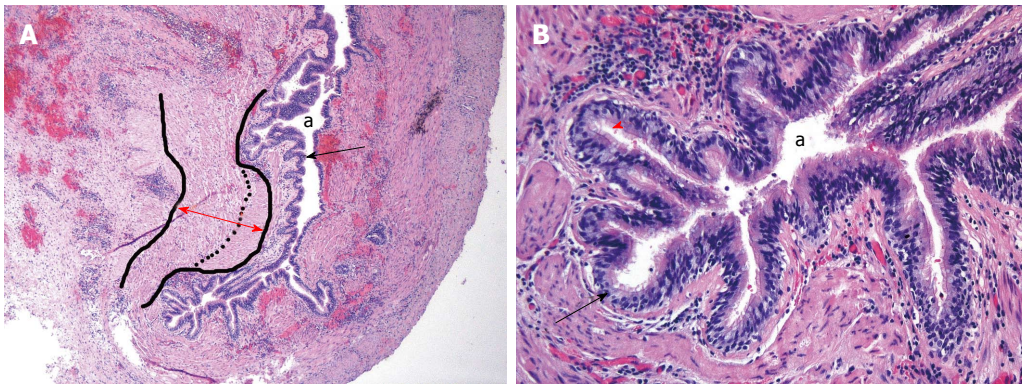

Figure 4 Histological findings of the cyst (hematoxylin/eosin staining). A: Magnification × 20; B: Magnification × 40. Indicated by numbers and arrows are the lining of respiratory epithelium (black arrows) with a muscularis propia consisting of two muscular layers (red arrow), the lumen of the cyst (a) and the ciliated pseudo stratified columnar epithelium (red arrowhead).

Table 1 Overview of published case reports of intra-abdominal esophageal duplication cysts

Ref.	Year	Patients age	Sex	Symptoms	Location of cyst	Size (cm)	Treatment
Pujar *et al*[1]	2013	13	F	Pain in epigastric region	Gastroesophageal junction, adjacent to left liver lobe	4.0 × 5.0	Laparoscopic resection
Bhamidipati *et al*[7]	2013	69	M	Weight loss, incidental at CT for diverticulitis	Gastroesophageal junction	4.4 × 3.7 × 3.9	Laparoscopic resection
Gümüş *et al*[8]	2011	18	F	At CT for dyspeptic complaints	Lower end of the esophagus, adjecent to liver	4.2 × 3.6	Open resection
Aldrink *et al*[2]	2011	2	M	No symptoms. Incidental at fundoplication	Gastroesophageal junction	3.0	Laparoscopic resection, with fundoplication
Martin *et al*[5]	2007	60	M	Gastric outlet obstruction	Retro-duodenal	10.0 × 10.0	Open resection
Martin *et al*[5]	2007	50	F	Left flank pain	Inferior to pancreatic tail	6.5 × 5.5 × 4.2	Open resection
Kin *et al*[9]	2003	51	F	No symptoms: incidental at staging CT for breastcancer	Diafragmatic crura	4.5 × 4.0 × 3.5	Laparoscopic resection with intra-operative esophagoscopy
Noguchi *et al*[10]	2003	26	F	Anal bleeding: incidental at ultrasound	Anterior wall of distal esophagus	4.0 × 3.0 × 3.0	Laparoscopic resection with esophageal repair(nissen)
Vijayaragh *et al*[11]	2002	70	F	Retching, rigidness and headache, incidental at ultrasound	Midline between stomach and liver	7.5	Open resection, combined with cholecystectomie
Nelms *et al*[4]	2002	44	M	Low back pain: incidental at CT	Diaphragmatic crura	7.0	Laparoscopic resection
Rathaus *et al*[12]	2000	5	F	Epigastric pain, ultrasound	Distal esophagus, between liver and cardia	1.0	Open resection
Janssen *et al*[13]	1998	56	F	Incidental at staging CT for rectal cancer	Superior to left kidney	8.0 × 6.0 × 4.5	Open resection
Karahasanoglu *et al*[14]	1997	51	M	Epigastric pain, dysphagia	Sub-diaphragmatic	11.0 × 9.0 × 8.0	Esophagogastrectomy
Harvell *et al*[15]	1996	57	F	Epigastric pain	Superior border of pancreas	2.2 × 1.7 × 1.5	Laparoscopic resection
Ruffin *et al*[16]	1989	38	F	Epigastric pain, nausea	Distal esophagus	4.0	Resection with esophageal repair

M: Male; F: Female; CT: Computed tomography.

Table 1 shows an overview of the abdominal cases that have been published so far. This overview shows that most cysts were asymptomatic and found incidental. In case of symptoms the most common complaint was epigastrical pain. In all cases the cyst was surgically removed, of which nearly 50% by means of laparoscopy. Four cases appeared in minors, 11 cases in adults. The median age at diagnosis was 50 years.

Besides the location of the cyst, a differentiation between the origin of the cyst can be made. Although it might not have clinical relevance in case of an asymptomatic cyst, the origin can be bronchogenic, esophageal, gastroenteric, neurenteric or pericardial. The latter three are histologically easy to differentiate. Gastroenteric and neurenteric cysts are lined with gastric mucosa and pericardial cysts are lined with flattened mesothelium. The difference between a bronchogenic and esophageal cyst is more difficult since both derive from the foregut and

contain ciliated epithelium. To differentiate bronchogenic from esophageal duplication cysts, Palmer's pathologic criteria are useful. These criteria include: (1) attachment to the esophageal wall; (2) presence of gastrointestinal tract epithelium; and (3) presence of two layers of muscularis propria[5]. Duplication cysts of bronchogenic origin do not have these two layers of smooth muscle, instead they contain cartilage, bronchogenic glands or both.

In intra-abdominal esophageal duplication cysts Palmer's criteria are not always applicable[4]. For example, in 2007 Martin *et al*[5] presented two cases of isolated intra-abdominal esophageal duplication cyst with no connection to any luminal organ.

The majority (80%) of esophageal duplication cysts becomes symptomatic during childhood and will be removed for that reason[1]. As a consequence these types of cysts are rarely seen in adults. If they are found during adulthood, they are mostly asymptomatic and most case reports are therefore based on an incidental finding during some kind of routine radiological investigation. However cysts can become symptomatic, like in our patient, causing abdominal pain, vomiting, dysphagia or reflux[1,2]. The growing cyst may also cause some mechanical problems of the passage of solid food and fluids because of compression of the esophagus[2]. Finally these cysts can perforate, they can cause an upper gastrointestinal bleeding or can get infected. Although a causal relationship is difficult to define, one case report has described a patient with a duplication cyst with an associated intracystic malignancy[6]. Because of these complications it is recommended to excise the cyst, whether it is symptomatic or not.

In our patient, symptoms of colic-like abdominal pain were initially addressed to symptomatic cholecystolithiasis, but eventually an esophageal duplication cyst appeared to be the actual cause of his symptoms. Although these cysts are very rare and mostly asymptomatic, they can mimic symptoms of common gastro-intestinal conditions. Therefore, one should consider these anomalies as a possible diagnosis if more obvious causes are excluded.

COMMENTS

Case characteristics

A 20-year-old male with a history of a cholecystectomy presents with colic like symptoms mimicking a cholecystolithiasis.

Clinical diagnosis

No abnormalities were found during physical examination, especially no pain during palpation of the right upper region of the abdomen.

Differential diagnosis

Choledocholithiasis, urolithiasis, esophageal duplication cyst

Laboratory diagnosis

Lab results showed no abnormalities in particular no signs of inflammation nor infection.

Imaging diagnosis

Computed tomography-scan and endoscopic ultrasonography (EUS) showed a 3.2 cm × 2.8 cm sized smooth lined lesion in the distal esophagus just below the diaphragm.

Pathological diagnosis

Histopathological analysis of the specimen revealed a 30 mm × 30 mm × 25 mm esophageal duplication cyst filled with clear fluid and a double muscular layer lined with respiratory columnar epithelium without any signs of cartilage.

Treatment

Laparoscopic excision of this cyst was performed.

Related reports

An esophageal duplication cyst is a rare diagnosis and is often asymptomatic.

Term explanation

An EUS is an endoscopic ultrasonography, which is an ultrasound made through the esophagus.

Experiences and lessons

Although these cysts are very rare and mostly asymptomatic, they can mimic symptoms of common gastro-intestinal conditions. Therefore, one should consider these anomalies as a possible diagnosis if more obvious causes are excluded.

Peer review

The paper describes a rare case of a symptomatic intra-abdominal esophageal duplication cyst and gives a complete overview of published cases until now. This case is very interesting for gastrointestinal surgeons well written and concise.

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CASE REPORT

Repair of an aberrant subclavian arterioesophageal fistula following esophageal stent placement

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Abstract

A fistula formation between the esophagus and an aberrant right subclavian artery is a rare but fatal complication that has been mostly described in the setting of prolonged nasogastric intubation and foreign body erosion. We report a case of a young morbidly obese patient who underwent sleeve gastrectomy that was complicated by a postoperative leak at the level of the gastroesophageal junction. A covered esophageal stent was placed endoscopically to treat the leak. The patient developed massive upper gastrointestinal bleeding secondary to the erosion of the stent into an aberrant retroesophageal right subclavian artery twelve days after stent placement. She was ultimately treated by endovascular stenting of the aberrant right subclavian artery followed by thoracotomy and esophageal repair over a T-tube. This case report highlights the multidisciplinary approach needed to diagnose and manage such a devastating complication. It also emphasizes the need for imaging studies prior to stent deployment to delineate the vascular anatomy and rule out the possibility of such an anomaly in view of the growing popularity of esophageal stents, especially in the setting of a leak.

Key words: Aberrant subclavian artery; Arterioesophageal fistula; Esophageal stent; Esophageal repair; Angioplasty; Sleeve gastrectomy; Leak

Core tip: The use of esophageal covered stents to treat leaks following sleeve gastrectomy has increased significantly over the past years. However, their possible complications have not yet been fully explored. As demonstrated by our case report, the presence of an aberrant retroesophageal Subclavian artery can predispose to the formation of a fistula with the esophagus secondary to stent erosion, thereby leading to catastrophic hemorrhage and death. Our approach in this case was to start with stent angioplasty of the Subclavian artery followed by thoracotomy and esophageal repair over a T-tube and this approach proved successful in saving the patient's life.

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INTRODUCTION

Aorto-esophageal and arterial-esophageal fistulae have both been described in the literature. These usually arise in the setting of arterial aneurysms and esophageal malignancy. An aberrant subclavian arterioesophageal fistula,

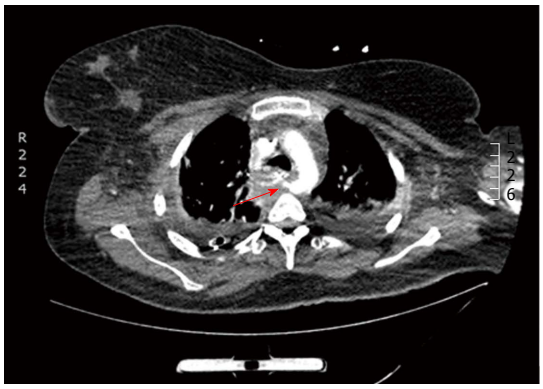

Figure 1 Computed tomography angiography showing a retroesophageal right suclavian artery with a pseudoaneurysm (arrow) around 1cm from its takeoff.

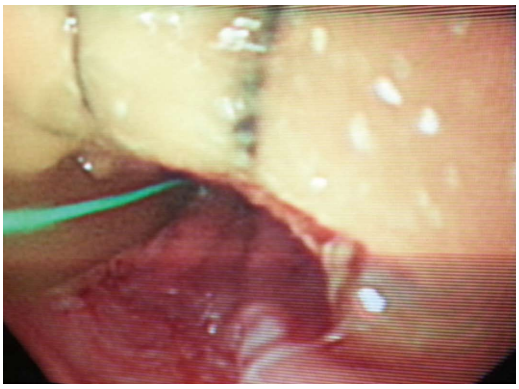

Figure 2 Upper endoscopy showing a 2 cm × 3 cm Teflon patch 22 cm from the incisor.

on the other hand, is an exceedingly rare occurrence and has been mostly reported in association with prolonged nasogastric intubation and erosion of esophageal instrumentation into the retroesophageal vessel. The mortality rate in such cases is extremely high as the bleeding is usually massive and sudden and ultimately leads to hemorrhagic shock and death. There are only a handful of reported cases of successful management of such a fistula. This paper describes the case of a young female who developed this devastating complication following the placement esophageal covered stent to treat a leak after sleeve gastrectomy. It also highlights the multidisciplinary approach used to diagnose and treat this complication.

CASE REPORT

A 29-year-old morbidly obese female developed a leak at the gastroesophageal junction following laparoscopic sleeve gastrectomy and underwent jejunostomy feeding tube insertion to allow spontaneous closure of the fistula. A gastrografin swallow performed a month later showed persistence of the leak. The patient then underwent an uneventful endoscopic stenting to exclude the leak and was discharged home on the same day. Twelve days later, she developed massive hematemesis and was taken to a district general hospital in a state of shock, where she was intubated and resuscitated. She underwent endoscopic removal of the stent followed by right thoracotomy, esophageal exploration and suturing of the fistula opening from the esophageal mucosal side thus obliterating and controlling the bleeding, followed by primary repair of the esophagus. Twelve hours later, the patient had a second episode of massive upper gastrointestinal (GI) bleeding and was in shock. She was taken back to the operating room where she was re-explored through a right thoracotomy. The esophagus was opened again and the bleeding site at the posterior wall of the esophagus was overrun and buttressed with a Teflon patch. She received a total of 29 units of packed red blood cells and 15 units of fresh frozen plasma. She was transferred to the intensive care unit at our medical center in critical condition. Computed tomography (CT) angiography revealed the presence of an esophageal perforation and a large pseudoaneurysm involving a right aberrant subclavian artery but there was no evidence of active bleeding at that point in time (Figure 1). Upper endoscopy revealed the presence of a Teflon patch within the lumen of the esophagus. The Teflon patch measured 2 cm × 3 cm and was placed at 22 cm from the incisors (Figure 2). After stabilizing the patient, she was taken to the interventional radiology suite for endovascular stenting and exclusion of the subclavian pseudoaneurysm to be followed by definitive surgical repair of the esophagus. Thoracic aorta angiography was performed and it revealed the presence of a right aberrant subclavian artery and a diverticulum of Kommerell as well as a 7 mm pseudoaneurysm approximately 1 cm from the origin of the right aberrant subclavian artery (Figure 3A). A right brachial artery cut down was then performed and a 6F sheath was used to deploy an 8 mm × 38 mm ATRIUM covered stent over the targeted area. Sequential balloon dilatation of the stent was then performed using 12 mm × 2 mm and 12 mm × 3 mm balloons and completion angiography demonstrated total occlusion of the pseudoaneurysm (Figure 3B). Following angioplasty, a right posterolateral thoracotomy with esophageal exploration was performed. The esophagotomy site was located above the division of the azygous vein. It was opened longitudinally and the Teflon patch was released from the posterior wall of the esophagus on the mucosal side (Figure 4). There was no evidence of bleeding through the surgically obliterated fistulous opening. The esophagus and its mucosa looked healthy and therefore primary closure over a 19F T-tube was performed. The esophagotomy was closed as a single layer using interrupted Polydioxanone sutures and was then buttressed with a fourth intercostal muscle flap.

The patient had a complicated postoperative course as she developed Acute Respiratory Distress Syndrome and was kept on mechanical ventilation for 10 d. She was fed through the previously inserted jejunostomy feeding tube. A gastrografin swallow performed two weeks after her surgery showed no evidence of contrast leak at the level of the esophageal repair (Figure 5). She was discharged home 33 d after her last operation. Twelve weeks later, the T tube was removed and she was started

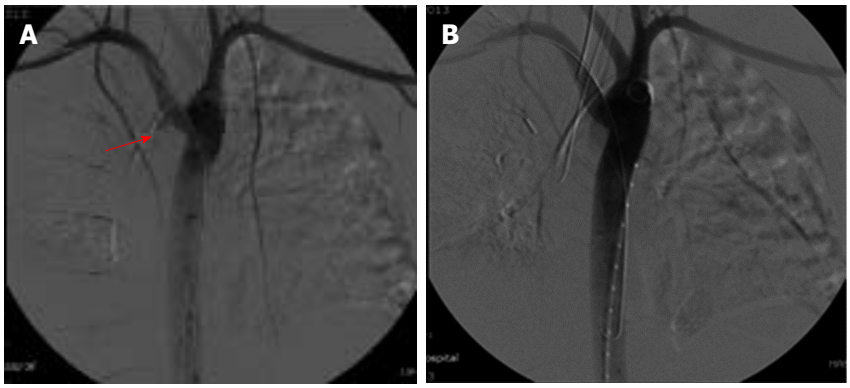

Figure 3 Thoracic aortic angiography. A: Showing the pseudoaneurysm (arrow); B: Angiography after stent deployment.

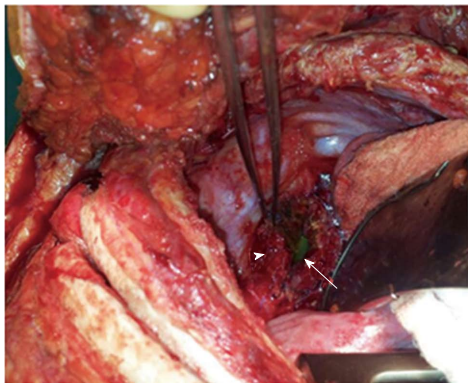

Figure 4 Thoracotomy with the Teflon patch (arrowhead) and nasogastric tube (arrow) visible through the esophagotomy.

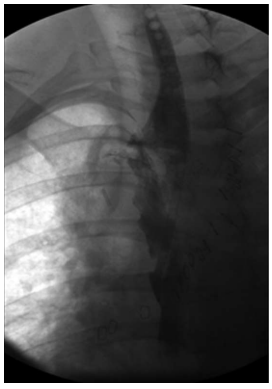

Figure 5 Gastrografin swallow performed postoperatively showing no evidence of a contrast leak at the site of the esophageal repair.

on regular oral feeding after a CT scan with oral contrast revealed no evidence of contrast extravasation (Figure 6).

DISCUSSION

An aberrant retroesophageal subclavian artery, also known as arteria lusoria, is the most common aortic arch anomaly. It has an incidence of 0.2% to 2% in the general population and is even more prevalent in patients with Down syndrome[1]. The persistence of the right dorsal aorta (known as Kommerell's diveritculum) and involution of the right 4th embryologic arch causes the advent of an aberrant right subclavian artery (ARSA)[2]. It is usually asymptomatic but may cause dysphagia (dysphagia lusoria) and may demonstrate symptomatic atherosclerotic and aneurysmal degeneration[3].

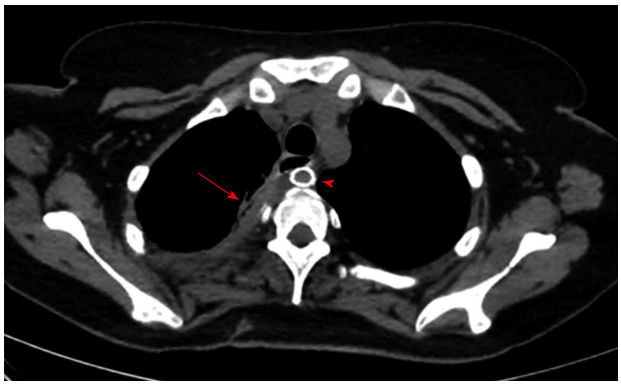

Figure 6 Computed tomography scan with oral contrast done after removal of the T-Tube with both the remnant tract of the T-tube (arrow) and the subclavian artery stent (arrowhead) seen.

Aorto-esophageal, arterial-esophageal, and aorto-enteric fistulae have all been described in the literature mainly in the setting aortic aneurysms, aortitis, atherosclerosis, and gastrointestinal malignancies[4]. Such fistulae have also been described in otherwise healthy people secondary to sharp trauma to the esophagus after swallowing animal bones, dentures, coins and other sharp objects[5]. A fistula between the esophagus and an ARSA, however, remains an exceptional event that has mostly been described in association with prolonged NG intubation[6]. The abnormal anatomic proximity to the esophagus or trachea likely renders the aberrant subclavian artery vulnerable to extrinsic compression and pressure necrosis by indwelling NG or endotracheal (ET) tubes[7]. The sequence of events may involve occlusion and thrombosis of the vasa vasorum, leading to vessel wall infarction and eventual wall dissolution. Moreover, ischemia and bacterial invasion of the vessel wall have also been suggested as important etiologic factors[8]. Unlike aorto-esophageal fistulae which present with sentinel bleeding in around 63% of cases, ARSA-esophageal fistulae present with

massive upper GI bleeding with an associated mortality approaching 100%[5]. As such, early diagnosis is of paramount importance.

In our literature review, we were able to find 17 reported cases of ARSA-esophageal fistulae out of which, only 4 patients survived the acute event[9-12]. In all reported cases, bleeding was sudden, unheralded by prior symptoms, and massive. In the surviving patients, the upper GI bleeding was controlled by a multidisciplinary approach consisting of endoscopic balloon compression or angiographic control or both, and the definitive therapy was provided by urgent surgery. Described successful surgical interventions include ligation of the subclavian artery after angiographic or endoscopic control followed mostly by subclavian artery bypass. Left thoracotomy has been advocated for satisfactory control of the aorta and ligation of the origin of the ARSA, but other recommendations include right thoracotomy for optimal exposure for both the arterial resection and the esophageal repair[10]. Miller *et al*[9] described the first successful repair of such a fistula in a young girl who developed massive hematemesis two weeks after insertion of an Endotracheal (ET) and NG tubes. She underwent left thoracotomy with esophagotomy and intraesophageal balloon tamponade by positioning a 30F Foley catheter at the bleeding point to control the hemorrhage and allow the patient to be stabilized hemodynamically. Following that, aortic arch arteriography through a right femoral approach was performed demonstrating an aberrant right subclavian artery as well as contrast extravasation consistent with a fistula between the anomalous vessel and the esophagus. The involved segment of the aberrant vessel was then ligated and resected via right thoracotomy, and the esophagus was repaired primarily. No revascularization of the right upper extremity was performed and the patient was reported to be symptom free. A similar successful repair was reported by Feugier *et al*[10] in which a 24-year-old male with prolonged Intensive Care Unit stay following polytrauma developed massive upper GI bleeding 31 d after insertion of ET and NG tubes. Urgent CT angiography revealed an ARSA in direct contact with the NG tube. Angiography was then performed through the right brachial artery confirming contrast extravasation and the bleeding was controlled by inflating a 7 mm × 20 mm balloon. The patient then underwent left anterolatral thoracotomy with ligation of the subclavian origin and carotid to subclavian bypass.

Embolization of the bleeding vessel has been described but it may not always be successful in stopping the bleeding and may even create further complications. This was demonstrated by Vanden Eynden *et al*[11] in a patient with an esophageal stent that was placed to manage an esophageal stricture and eroded into a retroesophageal subclavian artery. Attempted endovascular coil embolization failed to control the bleeding vessel and the patient underwent urgent exploration with ligation of the artery at its takeoff while the endoesophageal prosthesis was left in place followed by construction of an aorto-axillary bypass using an 8-mm polytetrafluoroethylene graft constructed between the lateral aspect of the ascending aorta and the axillary artery. Postoperative endoscopy revealed erosion of the deployed endovascular coils into the lumen of the esophagus.

Complete endovascular repair with covered stents without dividing the fistulous tract theoretically carries a risk of graft infection and should be reserved to extremely critical patients when a rapid and minimally invasive procedure could positively affect patient's outcome. Magagna *et al*[12] reported the placement of a 14 mm endovascular prosthesis in an ARSA to cover a fistula between the artery and the oesophagus in an elderly female with a tracheostomy and history of laryngectomy and radiotherapy who presented with massive upper GI bleeding. The procedure was performed after the bleeding was controlled by positioning a Sengstaken-Blakemore tube and the patient was stabilized.

The surgical rationale followed in our case which included stenting of the artery followed by thoracotomy and primary esophageal repair over T tube and buttressing with an intercostal muscle flap has never been attempted in the literature but appears to be an equally effective and successful option. Although our patient' s initial operation to control her bleeding stabilized her enough to allow for endovascular stenting of the pseudoaneurysm, it also necessitated another esophageal exploration for removal of the prosthetic patch and definitive esophageal repair. As the patient had two previous thoracotomies, it was of paramount importance to make sure that the esophageal repair is solid and to rule out a communication between the posterior wall of the esophagus and the stent that was placed in the subclavian artery. The Teflon patch that was previously placed in the lumen of the esophagus prevented us from assessing the posterior lumen of the esophagus and the integrity of the esophageal wall. It is also important to point to the fact that our patient had a sleeve gastrectomy, which precluded the option of using the stomach as conduit in the future should the esophageal repair fail. It was therefore extremely important to preserve the esophagus and as such, exploration and repair over a T-tube rather than a diverting cervical esphagostomy seemed the only treatment option.

ARSA-esophageal fistula is a rare but devastating complication of prolonged esophageal stenting and intubation and should be included in the differential diagnosis when investigating upper GI bleeding in patients with prolonged NG and ET intubation. It requires a multidisciplinary approach of different specialties including general and cardiothoracic surgery, interventional radiology, vascular surgery and intensive care. Angiography is an essential diagnostic and therapeutic tool as endoluminal balloons and stent grafts can be used as temporizing measures when feasible. Thoracotomy with ligation of the bleeding vessel and repair of the esophagotomy followed by revascularization of the right arm appears to be the most successful approach described in the literature. However, as demonstrated in our case, endovascular stenting of the fistulous tract followed by esophageal re-

pair offers an alternate effective treatment modality. Taking into account the poor survival after massive bleeding caused by an esophageal stent erosion into a major mediastinal vessels, and given the fact that esophageal stenting is gaining ground in the management of esophageal and gastroesophageal junction leaks post bariatric surgery[13], we recommend CT angiography of the chest to rule out the presence of the not uncommon ARSA in patients considered for prolonged esophageal stent placement.

COMMENTS

Case characteristics

Twenty-nine years old obese female with history of leak following sleeve gastrectomy underwent esophageal stent placement.

Clinical diagnosis

Massive upper gastrointestinal bleeding with hemorrhagic shock 12 d after stent placement.

Differential diagnosis

Bleeding gastric ulcer, esophageal bleeding, erosion of the stent into a major vessel.

Laboratory diagnosis

White blood cells 10.1 k/μL; HGB 6 mg/dL; hematocrit 18%; the electrolytes and metabolic panel were within normal limits.

Imaging diagnosis

Computed tomography angiography showed a communication between the esophagus and an aberrant retroesophageal right subclavian artery around 1 cm from the takeoff of the artery.

Pathological diagnosis

The esophageal covered stent eroded through the layers of the esophagus posteriorly reaching the aberrant Subclavian artery.

Treatment

Endovascular stenting of the Subclavian artery was first performed followed by thoracotomy and repair of the esophageal perforation over a T tube with intercostal muscle flap coverage.

Related reports

Aberrant right Subclavian rterioesophageal fistulas have been reported in the setting of prolonged nasogastric and endotracheal intubation causing erosion of the tube through the esophageal wall into the adjacent vessel with a high associated mortality rate.

Term explanation

An aberrant right Subclavian artery describes an anatomic variant in which the right Subclavian artery arises distal to the left Subclavian artery and courses behind the esophagus.

Experiences and lessons

This case report is the fifth reported case in literature of successful treatment of an aberrant subclavian arterioesophageal fistula. This was achieved by adopting a multidisciplinary approach spanning over different medical and surgical specialties. To prevent such a devastating complication, computed tomography angiography should be done to rule out the presence of an aberrant retroesophageal artery when contemplating the use of an esophageal stent for a prolonged period of time.

Peer review

The case is very interesting and the subject clinically relevant. The manuscript is well written and the images are nice. The subject is nicely reviewed in the discussion.

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INSTRUCTIONS TO AUTHORS

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WJGS covers topics concerning micro-invasive surgery; laparoscopy; hepatic, biliary, pancreatic and splenic surgery; surgical nutrition; portal hypertension, as well as associated subjects. The current columns of *WJGS* include editorial, frontier, diagnostic advances, therapeutics advances, field of vision, mini-reviews, review, topic highlight, medical ethics, original articles, case report, clinical case conference (clinicopathological conference), and autobiography. Priority publication will be given to articles concerning diagnosis and treatment of gastrointestinal surgery diseases. The following aspects are covered: clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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Chinese journal article (list all authors and include the PMID where applicable)

2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarrhoea. *Shijie Huaren Xiaohua Zazhi* 1999; **7**: 285-287

In press

3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

Organization as author

4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

Books

Personal author(s)

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flex-

ible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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Write as mean ± SD or mean ± SE.

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